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Trying 3106016892...Open

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Dec 17 The CA Lexicon available in the CAPLUS and CA files
NEWS 3 Feb 06 Engineering Information Encompass files have new names
NEWS 4 Feb 16 TOXLINE no longer being updated
NEWS 5 Apr 23
                Search Derwent WPINDEX by chemical structure
NEWS 6 Apr 23 PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7 May 07
                DGENE Reload
                Published patent applications (A1) are now in USPATFULL
NEWS 8 Jun 20
NEWS 9 JUL 13
                New SDI alert frequency now available in Derwent's
                DWPI and DPCI
NEWS 10 Aug 23
                In-process records and more frequent updates now in
                MEDLINE
                PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
NEWS 11 Aug 23
NEWS 12 Aug 23
                Adis Newsletters (ADISNEWS) now available on STN
NEWS 13 Sep 17
                IMSworld Pharmaceutical Company Directory name change
                to PHARMASEARCH
NEWS 14 Oct 09
                Korean abstracts now included in Derwent World Patents
                Index
NEWS 15 Oct 09
                Number of Derwent World Patents Index updates increased
NEWS 16 Oct 15 Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17 Oct 22 Over 1 million reactions added to CASREACT
NEWS 18 Oct 22
                DGENE GETSIM has been improved
NEWS 19 Oct 29 AAASD no longer available
NEWS EXPRESS August 15 CURRENT WINDOWS VERSION IS V6.0c,
             CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
             AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
             STN Operating Hours Plus Help Desk Availability
NEWS HOURS
NEWS INTER
             General Internet Information
NEWS LOGIN
             Welcome Banner and News Items
             Direct Dial and Telecommunication Network Access to STN
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Enter NEWS followed by the item number or name to see news on that specific topic.

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Connecting via Winsock to STN

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NEWS WWW

Welcome to STN International! Enter x: Welcome to STN International! Enter x:x LOGINID:SSSPTA1600RXM PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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Welcome to STN International
NEWS
                Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Dec 17
                The CA Lexicon available in the CAPLUS and CA files
                Engineering Information Encompass files have new names
NEWS 3 Feb 06
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        Jun 20
                Published patent applications (A1) are now in USPATFULL
NEWS 9
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                In-process records and more frequent updates now in
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NEWS 13 Sep 17
                IMSworld Pharmaceutical Company Directory name change
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NEWS HOURS
             General Internet Information
NEWS INTER
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Enter NEWS followed by the item number or name to see news on that specific topic.

Welcome Banner and News Items

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

CAS World Wide Web Site (general information)

Direct Dial and Telecommunication Network Access to STN

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FILE 'SCISEARCH' ENTERED AT 16:24:37 ON 02 NOV 2001 COPYRIGHT (C) 2001 Institute for Scientific Information (ISI) (R)

=> s fibronectin 100222 FIBRONECTIN

=> s fibrin (w) binding (w) domain 198 FIBRIN (W) BINDING (W) DOMAIN

=> s L1 and L2

135 L1 AND L2

=> s L1 and (marker or image or isotope or label) 6568 L1 AND (MARKER OR IMAGE OR ISOTOPE OR LABEL)

=> s L4 and fibrin

149 L4 AND FIBRIN

=> s L5 and ((thrombus or atherosclerotic (w) plaque)) 15 L5 AND ((THROMBUS OR ATHEROSCLEROTIC (W) PLAQUE))

=> s L5 and ((fibrin (w) binding (w) domain)) 17 L5 AND ((FIBRIN (W) BINDING (W) DOMAIN))

=> dup rem L6

PROCESSING COMPLETED FOR L6

11 DUP REM L6 (4 DUPLICATES REMOVED)

=> dup rem L7

PROCESSING COMPLETED FOR L7

L9 9 DUP REM L7 (8 DUPLICATES REMOVED)

=> dis L8 1-11 ibib kwic

ANSWER 1 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1 18

FILE 'HOME' ENTERED AT 16:23:05 ON 02 NOV 2001 => file biosis caplus embase medline scisearch

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=> s fibrin (w) binding (w) domain L2 198 FIBRIN (W) BINDING (W) DOMAIN

=> s L1 and L2 L3 135 L1 AND L2

=> s L1 and (marker or image or isotope or label)
L4 6568 L1 AND (MARKER OR IMAGE OR ISOTOPE OR LABEL)

=> s L4 and fibrin L5 149 L4 AND FIBRIN

=> s L5 and ((thrombus or atherosclerotic (w) plaque))

L6 15 L5 AND ((THROMBUS OR ATHEROSCLEROTIC (W) PLAQUE))

=> s L5 and ((fibrin (w) binding (w) domain)) L7 L5 AND ((FIBRIN (W) BINDING (W) DOMAIN))

=> dup rem L6

PROCESSING COMPLETED FOR L6

L8 11 DUP REM L6 (4 DUPLICATES REMOVED)

=> dup rem L7

PROCESSING COMPLETED FOR L7

L9 9 DUP REM L7 (8 DUPLICATES REMOVED)

=> dis L8 1-11 ibib kwic

L8 ANSWER 1 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1

ACCESSION NUMBER: 2001142593 EMBASE

TITLE: Radiolabeled peptides in the detection of deep venous

thrombosis.

AUTHOR: Taillefer R.

Dr. R. Taillefer, Department of Nuclear Medicine, CORPORATE SOURCE:

Hotel-Dieu de Montreal, 3840 rue St-Urbain, Montreal, H2W

1T8, Canada

SOURCE: Seminars in Nuclear Medicine, (2001) 31/2 (102-123).

Refs: 55

ISSN: 0001-2998 CODEN: SMNMAB

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review FILE SEGMENT: 023 Nuclear Medicine

037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

. . . and ultrasonography are imaging procedures that detect changes

venous anatomy that are caused by the presence of an intraluminal thrombus that is sufficiently formed either to reduce vascular filling with contrast medium or to resist compression. However, these imaging procedures. . . by various disease-related and technical factors. An alternative approach to the diagnosis of acute DVT is to detect a molecular marker of acute DVT that is not present in old, organized DVT. Recent advances in biotechnology permit the use of highly specific synthetic peptide or small molecular markers, which are involved in the acute stages of DVT formation and can be

labeled

efficiently with (99m)Tc. (99m)Tc-apcitide, a glycoprotein. . . acute DVT. Two other agents are currently under clinical investigation: (99m)Tc-DMP 444, which is another GP IIb/IIIa receptor antagonist, and (99m)Tc-Fibrin-Binding Domain (FBD), a radio-labeled fibrin-binding domain of fibronectin. Different clinical

studies have shown a high diagnostic accuracy with these synthetic (99m)Tc-labeled peptides in the detection of acute DVT.. . .

Medical Descriptors:

*deep vein thrombosis: DI, diagnosis

*protein analysis

isotope labeling

peptide analysis diagnostic value reliability

color ultrasound flowmetry

biotechnology drug mechanism

human

human tissue human cell review

*fibronectin: EC, endogenous compound

*fibrinogen receptor antagonist: PD, pharmacology

*technetium 99m

(fibronectin) 86088-83-7; (technetium 99m) 14133-76-7 RN

ANSWER 2 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 2001:225518 BIOSIS DOCUMENT NUMBER: PREV200100225518

Fibrin binding domain polypeptides and uses and TITLE:

2001142593 EMBASE ACCESSION NUMBER:

Radiolabeled peptides in the detection of deep venous TITLE:

thrombosis.

AUTHOR: Taillefer R.

Dr. R. Taillefer, Department of Nuclear Medicine, CORPORATE SOURCE:

Hotel-Dieu de Montreal, 3840 rue St-Urbain, Montreal, H2W

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Seminars in Nuclear Medicine, (2001) 31/2 (102-123). SOURCE:

Refs: 55

ISSN: 0001-2998 CODEN: SMNMAB

United States COUNTRY:

Journal; General Review DOCUMENT TYPE: FILE SEGMENT: 023 Nuclear Medicine 037 Drug Literature Index

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*technetium 99m

(fibronectin) 86088-83-7; (technetium 99m) 14133-76-7 RN

ANSWER 2 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 2001:225518 BIOSIS DOCUMENT NUMBER: PREV200100225518

TITLE: Fibrin binding domain polypeptides and uses and methods of producing same.

Vogel, Tikv (1); Levanon, Avigdor; Werber, Moshe; Guy, AUTHOR(S):

Rachel; Panet, Amos

CORPORATE SOURCE: (1) Rehovot Israel

ASSIGNEE: Bio-Technology General Corp. PATENT INFORMATION: US 6121426 September 19, 2000

Official Gazette of the United States Patent and Trademark SOURCE:

Office Patents, (Sep. 19, 2000) Vol. 1238, No. 3, pp. No

Pagination. e-file. ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

Fibrin binding domain polypeptides and uses and methods of ΤI

producing same.

AB This invention provides an imaging agent which comprises a polypeptide labeled with an imageable marker, such polypeptide having an amino acid sequence substantially present in the fibrin binding domain of naturally-occurring human fibronectin and being capable of binding to fibrin. The invention further provides a method wherein the imaging agent is used for imaging a fibrin -containing substance, i.e., a thrombus or

atherosclerotic plaque. Further provided are plasmids for expression of polypeptides having an amino acid sequence substantially

present in the fibrin binding domain of naturally-occurring human fibronectin and being capable of binding to fibrin

, hosts containing these plasmids, methods of producing the polypeptides, methods of treatment using the polypeptides, and methods of recovering, refolding. . . purified polypeptides substantially free of other

substances of human origin which have an amino acid sequence substantially

present in the fibrin binding domain of naturally-occurring human fibronectin and which are capable of binding to fibrin.

IT Major Concepts

Biochemistry and Molecular Biophysics; Radiology (Medical Sciences)

Chemicals & Biochemicals IT

fibrin binding domain polypeptides: imaging agents

Miscellaneous Descriptors TT

fibrin-containing domain

ANSWER 3 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS

2000:277499 BIOSIS ACCESSION NUMBER: DOCUMENT NUMBER: PREV200000277499

Fibrin binding domain polypeptides and uses and TITLE:

methods of producing same.

AUTHOR(S): Vogel, Tikv (1); Levanon, Avigdor; Werber, Moshe; Guy,

> Rachel; Panet, Amos (1) Rehovot Israel

CORPORATE SOURCE:

ASSIGNEE: Bio-Technology General Corp., Iselin, NJ, USA

PATENT INFORMATION: US 5965383 October 12, 1999

Official Gazette of the United States Patent and Trademark SOURCE:

Office Patents, (Oct. 12, 1999) Vol. 1227, No. 2, pp. No.

pagination. e-file..

ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

TΙ Fibrin binding domain polypeptides and uses and methods of methods of producing same.

Vogel, Tikv (1); Levanon, Avigdor; Werber, Moshe; Guy, AUTHOR(S):

Rachel; Panet, Amos

(1) Rehovot Israel CORPORATE SOURCE:

ASSIGNEE: Bio-Technology General Corp.

PATENT INFORMATION: US 6121426 September 19, 2000

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Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 19, 2000) Vol. 1238, No. 3, pp. No.

Pagination. e-file. ISSN: 0098-1133.

DOCUMENT TYPE:

Patent English

LANGUAGE:

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This invention provides an imaging agent which comprises a polypeptide AB labeled with an imageable marker, such polypeptide having an amino acid sequence substantially present in the fibrin binding domain of naturally-occurring human fibronectin and being capable of binding to fibrin. The invention further provides a method wherein the imaging agent is used for imaging a fibrin -containing substance, i.e., a thrombus or

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present in the fibrin binding domain of naturally-occurring human fibronectin and being capable of binding to fibrin , hosts containing these plasmids, methods of producing the polypeptides, methods of treatment using the polypeptides, and methods of recovering, refolding. . . purified polypeptides substantially free of other substances of human origin which have an amino acid sequence substantially

present in the fibrin binding domain of naturally-occurring human fibronectin and which are capable of binding to fibrin.

ΙT Major Concepts

Biochemistry and Molecular Biophysics; Radiology (Medical Sciences)

Chemicals & Biochemicals TΤ

fibrin binding domain polypeptides: imaging agents

ΙT Miscellaneous Descriptors

fibrin-containing domain

ANSWER 3 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS

2000:277499 BIOSIS ACCESSION NUMBER: PREV200000277499 DOCUMENT NUMBER:

TITLE: Fibrin binding domain polypeptides and uses and

methods of producing same.

AUTHOR(S): Vogel, Tikv (1); Levanon, Avigdor; Werber, Moshe; Guy,

Rachel; Panet, Amos

(1) Rehovot Israel CORPORATE SOURCE:

ASSIGNEE: Bio-Technology General Corp., Iselin, NJ, USA

PATENT INFORMATION: US 5965383 October 12, 1999

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DOCUMENT TYPE:

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LANGUAGE: English

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substantially

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present in the **fibrin** binding domain of naturally-occurring human **fibronectin** and which are capable of binding to **fibrin**.

IT Major Concepts

Biochemistry and Molecular Biophysics; Cardiovascular Medicine (Human Medicine, Medical Sciences); Methods and Techniques

IT Chemicals & Biochemicals

fibrin; polypeptide: fibrin binding domain, imaging
agent

IT Methods & Equipment

imaging method: imaging method

IT Miscellaneous Descriptors

atherosclerotic plaque; thrombus

L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:9677 CAPLUS

DOCUMENT NUMBER: 130:78109

TITLE: Application of 13C-13C, 13C-15N, and 13C-13C-15N

isotopically enriched proteins as tissue-directed

image-enhancement reagents for magnetic

resonance imaging

INVENTOR(S): Montelione, Gaetano T.; Stein, Stanley

PATENT ASSIGNEE(S): University of Medicine & Dentistry of New Jersey,

USA;

SOURCE:

Rutgers University PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9857578 Al 19981223 WO 1998-US12568 19980617

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

producing same.

AB This invention provides an imaging agent which comprises a polypeptide labeled with an imageable marker, such polypeptide having an amino acid sequence substantially present in the fibrin binding domain of naturally-occurring human fibronectin and being capable of binding to fibrin. The invention further provides a method wherein the imaging agent is used for imaging a fibrin -containing substance, i.e., a thrombus-or

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 for expression of polypeptides having an amino acid sequence
substantially

present in the **fibrin** binding domain of naturally-occurring human **fibronectin** and being capable of binding to **fibrin**, hosts containing these plasmids, methods of producing the polypeptides, methods of treatment using the polypeptides, and methods of recovering, refolding. . . purified polypeptides substantially free of other substances of human origin which have an amino acid sequence substantially

present in the **fibrin** binding domain of naturally-occurring human **fibronectin** and which are capable of binding to **fibrin**.

IT Major Concepts

Biochemistry and Molecular Biophysics; Cardiovascular Medicine (Human Medicine, Medical Sciences); Methods and Techniques

IT Chemicals & Biochemicals

fibrin; polypeptide: fibrin binding domain, imaging
agent

IT Methods & Equipment

imaging method: imaging method

IT Miscellaneous Descriptors

atherosclerotic plaque; thrombus

L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1999:9677 CAPLUS

DOCUMENT NUMBER:

130:78109

TITLE:

Application of 13C-13C, 13C-15N, and 13C-13C-15N isotopically enriched proteins as tissue-directed

image-enhancement reagents for magnetic

resonance imaging

INVENTOR(S):

Montelione, Gaetano T.; Stein, Stanley

PATENT ASSIGNEE(S):

University of Medicine & Dentistry of New Jersey,

USA;

SOURCE:

Rutgers University PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.				KIND		DATE			APPLICATION NO.					DATE			
WO	WO 9857578			A1 19981223				WO 1998-US12568 19980617									
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                                        WO 1998-US12568 W
                                                            19980617
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                         (1) Bogdanov; US 5593658 A 1997
REFERENCE(S):
                         (2) Brixner; US 5094848 A 1992 CAPLUS
                         (3) Sinn; US 5308604 A 1994 CAPLUS
ΤI
     Application of 13C-13C, 13C-15N, and 13C-13C-15N isotopically enriched
     proteins as tissue-directed image-enhancement reagents for
     magnetic resonance imaging
TΤ
     Platelet (blood)
        (activated-platelet binding protein; carbon-13-carbon-13,
        carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15
isotopically
        enriched proteins as tissue-directed image-enhancement
        reagents for magnetic resonance imaging)
TΤ
     Nucleic acids
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (binding proteins for; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
ΙT
    MRI contrast agents
     Spin-spin relaxation
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Antigens
     Receptors
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Antibody conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
TT
     Monoclonal antibody conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Peptide conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Polymers, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Protein conjugates
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             CM, GA, GN, ML, MR, NE, SN, TD, TG
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PRIORITY APPLN. INFO.:
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                                        US 1997-63252
                                        WO 1998-US12568 W 19980617
REFERENCE COUNT:
REFERENCE(S):
                         (1) Bogdanov; US 5593658 A 1997
                         (2) Brixner; US 5094848 A 1992 CAPLUS
                         (3) Sinn; US 5308604 A 1994 CAPLUS
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     Application of 13C-13C, 13C-15N, and 13C-13C-15N isotopically enriched
     proteins as tissue-directed image-enhancement reagents for
     magnetic resonance imaging
TT
     Platelet (blood)
        (activated-platelet binding protein; carbon-13-carbon-13,
        carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15
isotopically
        enriched proteins as tissue-directed image-enhancement
        reagents for magnetic resonance imaging)
IT
     Nucleic acids
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (binding proteins for; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
IT
    MRI contrast agents
     Spin-spin relaxation
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Antigens
     Receptors
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Antibody conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Monoclonal antibody conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Peptide conjugates
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Polymers, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Protein conjugates
```

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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Proteins (general), biological studies
ΙT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
ΙT
     Organic compounds, biological studies
     Single chain antibodies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugates; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
IT
     Fibronectins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (fibrin-binding domain fragment; carbon-13-carbon-13,
        carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15
isotopically
        enriched proteins as tissue-directed image-enhancement
        reagents for magnetic resonance imaging)
IT
        (infectious agent antigen or receptor targeting group;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for MRI)
IT
     Proteins (specific proteins and subclasses)
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ligand-binding, nucleic acid- and protein-, conjugates;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
ΙT
     Fibrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (monoclonal antibodies to; carbon-13-carbon-13, carbon-13-nitrogen-15,
        and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
     .beta.-Amyloid
IT
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (plaque, targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15,
        and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
ΙT
     Thrombus
        (targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
ΤТ
    Antigens
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (tumor-specific antigens; carbon-13-carbon-13, carbon-13-nitrogen-15,
        and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
ΙT
    Alzheimer's disease
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```
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Proteins (general), biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Organic compounds, biological studies
IT
     Single chain antibodies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugates; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
IT
    Fibronectins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (fibrin-binding domain fragment; carbon-13-carbon-13,
        carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15
isotopically
        enriched proteins as tissue-directed image-enhancement
        reagents for magnetic resonance imaging)
IT
        (infectious agent antigen or receptor targeting group;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for MRI)
IT
     Proteins (specific proteins and subclasses)
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ligand-binding, nucleic acid- and protein-, conjugates;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
TΤ
     Fibrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (monoclonal antibodies to; carbon-13-carbon-13, carbon-13-nitrogen-15,
        and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
IT
     .beta.-Amyloid
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (plaque, targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15,
        and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
IT
     Thrombus
        (targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
IT
     Antigens
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (tumor-specific antigens; carbon-13-carbon-13, carbon-13-nitrogen-15,
        and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
     Alzheimer's disease
IT
```

enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

IT 108-77-0D, Cyanuric chloride, reaction products with tissue-directed targeting group and isotopically enriched protein 573-58-0D, Congo red, conjugates 3934-20-1D, 2,4-Dichloropyrimidine, reaction products with tissue-directed targeting group and isotopically enriched protein 14390-96-6, Nitrogen-15, biological studies 14762-74-4, Carbon-13, biological studies 20342-94-3D, reaction products with tissue-directed targeting group and isotopically enriched protein 58626-38-3D, reaction products with tissue-directed targeting group and isotopically enriched protein 218432-70-3D, conjugates

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

IT 139639-23-9, Tissue plasminogen activator

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inactivated, conjugates; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

L8 ANSWER 5 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

ACCESSION NUMBER: 1997:244476 BIOSIS DOCUMENT NUMBER: PREV199799543679

TITLE: Recombinant polypeptides derived from the fibrin

binding domain of fibronectin are potential

agents for the imaging of blood clots.

AUTHOR(S): Ezov, N.; Nimrod, A.; Parizada, B.; Erber, M. M.;

Goldlust,

A.; Greenstein, L. A.; Vogel, T.; Drizlich, N.; Levanon,

A.; Reich, S.; Gorecki, M.; Panet, A. (1)

CORPORATE SOURCE: (1) Bio-Technol. Gen., Kiryat Weizmann, Rehovot 76326

Israel

SOURCE: Thrombosis and Haemostasis, (1997) Vol. 77, No. 4, pp.

796-803.

ISSN: 0340-6245.

DOCUMENT TYPE: Article LANGUAGE: English

TI Recombinant polypeptides derived from the **fibrin** binding domain of **fibronectin** are potential agents for the imaging of blood clots.

Thrombus formation in the circulation is accompanied by covalent linkage of fibronectin (FN) through transglutamination of glutamine no. 3 in the fibrin binding amino terminal domain (FBD) of FN. We have exploited this phenomenon for thrombus detection by the employment of radioactively-labelled recombinant polypeptide molecules derived from the 5-finger FBD of human FN. Three recombinant FBD. . . FBD ("5 fingers"), were prepared and compared to native FN-derived 31 kDa-FBD with respect to their ability to attach to fibrin clots in vitro and in vivo. The accessibility of Gln-3 in these molecules was demonstrated by the incorporation of stoichiometric amounts of 14C-putrescine in the presence of plasma transglutaminase. Competitive binding experiments to fibrin have indicated that, although the binding affinities of the FBD molecules are lower than that

(.beta.-amyloid plaque targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically

> enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

108-77-0D, Cyanuric chloride, reaction products with tissue-directed ΙT targeting group and isotopically enriched protein 573-58-0D, Congo red, conjugates 3934-20-1D, 2,4-Dichloropyrimidine, reaction products with tissue-directed targeting group and isotopically enriched protein 14390-96-6, Nitrogen-15, biological studies 14762-74-4, Carbon-13, biological studies 20342-94-3D, reaction products with tissue-directed targeting group and isotopically enriched protein 58626-38-3D, reaction products with tissue-directed targeting group and isotopically enriched 218432-70-3D, conjugates

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

139639-23-9, Tissue plasminogen activator IT

> RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inactivated, conjugates; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

ANSWER 5 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

ACCESSION NUMBER:

1997:244476 BIOSIS

DOCUMENT NUMBER:

PREV199799543679

TITLE:

Recombinant polypeptides derived from the fibrin

binding domain of fibronectin are potential

agents for the imaging of blood clots.

AUTHOR(S):

Ezov, N.; Nimrod, A.; Parizada, B.; Erber, M. M.;

Goldlust,

A.; Greenstein, L. A.; Vogel, T.; Drizlich, N.; Levanon,

A.; Reich, S.; Gorecki, M.; Panet, A. (1)

CORPORATE SOURCE:

(1) Bio-Technol. Gen., Kiryat Weizmann, Rehovot 76326

Israel

SOURCE:

Thrombosis and Haemostasis, (1997) Vol. 77, No. 4, pp.

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ISSN: 0340-6245.

DOCUMENT TYPE:

Article

LANGUAGE:

English

- Recombinant polypeptides derived from the fibrin binding domain of fibronectin are potential agents for the imaging of blood
- Thrombus formation in the circulation is accompanied by covalent AΒ linkage of fibronectin (FN) through transglutamination of glutamine no. 3 in the fibrin binding amino terminal domain (FBD) of FN. We have exploited this phenomenon for thrombus detection by the employment of radioactively-labelled recombinant polypeptide molecules derived from the 5-finger FBD of human FN. Three recombinant FBD. . . FBD ("5 fingers"), were prepared and compared to native FN-derived 31 kDa-FBD with respect to their ability to attach to fibrin clots in vitro and in vivo. The accessibility of Gln-3 in these molecules was demonstrated by the incorporation of stoichiometric amounts of 14C-putrescine in the presence of plasma transglutaminase. Competitive binding experiments to fibrin have indicated that, although the binding affinities of the FBD molecules are lower than that

of FN, substantial covalent linkage. . . The potential of the 12 kDa and 31 kDa FBDs as imaging agents was examined in a stainless steel coil-induced **thrombus** model in rats and in a jugular vein **thrombus** model in rabbits, using either (125I) or (111In)labelled materials. At 24 h, clot-to-blood ratios ranged between 10 and 22 for.

IT Miscellaneous Descriptors

BLOOD AND LYMPHATIC DISEASE; BLOOD AND LYMPHATICS; FIBRIN RECOMBINANT POLYPEPTIDES; FIBRINOGEN; FIBRONECTIN; INDIUM-111 LABEL; IODINE-125 LABEL; POTENTIAL BLOOD CLOT IMAGING AGENT; RADIATION BIOLOGY; THROMBUS

L8 ANSWER 6 OF 11 SCISEARCH COPYRIGHT 2001 ISI (R)

ACCESSION NUMBER: 96:795436 SCISEARCH

THE GENUINE ARTICLE: VP508

TITLE: BACTERIAL ADHESION ON POLYURETHANE SURFACES CONDITIONED

WITH THROMBUS COMPONENTS

AUTHOR: BAUMGARTNER J N; COOPER S L (Reprint)

CORPORATE SOURCE: UNIV DELAWARE, DEPT CHEM ENGN, NEWARK, DE, 19716

(Reprint); UNIV DELAWARE, DEPT CHEM ENGN, NEWARK, DE,

19716

COUNTRY OF AUTHOR: USA

SOURCE: ASAIO JOURNAL, (SEP/OCT 1996) Vol. 42, No. 5, pp.

M476-M479.

ISSN: 1058-2916.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: CLIN LANGUAGE: ENGLISH

REFERENCE COUNT: 20

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

TI BACTERIAL ADHESION ON POLYURETHANE SURFACES CONDITIONED WITH THROMBUS COMPONENTS

AB . . . deposition occurs, as do activation of the blood coagulation cascade, platelet adhesion, activation, and aggregation, all of which lead

to thrombus formation. An increased incidence of bacterial infection also has been seen clinically with indwelling biomaterial devices. Some evidence suggests a possible association between thrombosis and infection, in that adherent bacteria may provide a nidus for thrombus formation, or adherent thrombi composed of platelets and fibrin may form sheltered sites for bacterial adhesion.(1,2) In the current study, the authors examined Staphylococcus aureus adhesion to sulfonated, aminated,. . . Bacterial adhesion was observed in a radial flow chamber mounted on the motorized stage of a video microscopy system, with image processing software used to perform automated data collection and image analysis. Scanning electron microscopy also was used to visualize cross-linked fibrin and bacterial adhesion on these surfaces. Bacterial adhesion was found to be lowest on the phosphonated polyurethane. The presence of fibrin or isolated platelets significantly increased bacterial adhesion compared to surfaces pre-adsorbed with albumin.

STP KeyWords Plus (R): STAPHYLOCOCCUS-AUREUS; MEDIATED ADHESION; FIBRONECTIN; INFECTION; ADHERENCE; EPIDERMIDIS; FIBRINOGEN; FLOW

L8 ANSWER 7 OF 11 MEDLINE

ACCESSION NUMBER: 94291101 MEDLINE

DOCUMENT NUMBER: 94291101 PubMed ID: 8020011

TITLE: [Imaging in atherosclerosis: scintigraphy techniques].

of FN, substantial covalent linkage. . . The potential of the 12 kDa and 31 kDa FBDs as imaging agents was examined in a stainless steel coil-induced thrombus model in rats and in a jugular vein thrombus model in rabbits, using either (1251) or (111In)labelled materials. At 24 h, clot-to-blood ratios ranged between 10 and 22 for.

IT Miscellaneous Descriptors

> BLOOD AND LYMPHATIC DISEASE; BLOOD AND LYMPHATICS; FIBRIN RECOMBINANT POLYPEPTIDES; FIBRINOGEN; FIBRONECTIN; INDIUM-111 LABEL; IODINE-125 LABEL; POTENTIAL BLOOD CLOT IMAGING AGENT; RADIATION BIOLOGY; THROMBUS

ANSWER 6 OF 11 SCISEARCH COPYRIGHT 2001 ISI (R)

ACCESSION NUMBER: 96:795436 SCISEARCH

THE GENUINE ARTICLE: VP508

TITLE: BACTERIAL ADHESION ON POLYURETHANE SURFACES CONDITIONED

WITH THROMBUS COMPONENTS

BAUMGARTNER J N; COOPER S L (Reprint) AUTHOR:

CORPORATE SOURCE: UNIV DELAWARE, DEPT CHEM ENGN, NEWARK, DE, 19716

(Reprint); UNIV DELAWARE, DEPT CHEM ENGN, NEWARK, DE,

19716

COUNTRY OF AUTHOR: USA

SOURCE: ASAIO JOURNAL, (SEP/OCT 1996) Vol. 42, No. 5, pp.

M476-M479.

ISSN: 1058-2916.

DOCUMENT TYPE:

Article; Journal

FILE SEGMENT:

CLIN ENGLISH

LANGUAGE:

REFERENCE COUNT: 20

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

BACTERIAL ADHESION ON POLYURETHANE SURFACES CONDITIONED WITH ΤI THROMBUS COMPONENTS

. . deposition occurs, as do activation of the blood coagulation AB cascade, platelet adhesion, activation, and aggregation, all of which lead

to thrombus formation. An increased incidence of bacterial infection also has been seen clinically with indwelling biomaterial devices. Some evidence suggests a possible association between thrombosis and infection, in that adherent bacteria may provide a nidus for thrombus formation, or adherent thrombi composed of platelets and fibrin may form sheltered sites for bacterial adhesion.(1,2) In the current study, the authors examined Staphylococcus aureus adhesion to sulfonated, aminated, . . . Bacterial adhesion was observed in a radial flow chamber mounted on the motorized stage of a video microscopy system, with image processing software used to perform automated data collection and image analysis. Scanning electron microscopy also was used to visualize cross-linked fibrin and bacterial adhesion on these surfaces. Bacterial adhesion was found to be lowest on the phosphonated polyurethane. The presence of fibrin or isolated platelets significantly increased bacterial adhesion compared to surfaces pre-adsorbed with albumin.

STP KeyWords Plus (R): STAPHYLOCOCCUS-AUREUS; MEDIATED ADHESION; FIBRONECTIN; INFECTION; ADHERENCE; EPIDERMIDIS; FIBRINOGEN; FLOW

ANSWER 7 OF 11 MEDLINE

ACCESSION NUMBER: 94291101 MEDLINE

DOCUMENT NUMBER: 94291101 PubMed ID: 8020011

TITLE: [Imaging in atherosclerosis: scintigraphy techniques]. Imaging nell'aterosclerosi: tecniche scintigrafiche.

Greco C; Scopinaro F; Centi Colella A; Campa P P AUTHOR:

CORPORATE SOURCE: II Cattedra di Cardiologia, Universita degli Studi La

Sapienza, Roma.

CARDIOLOGIA, (1993 Dec) 38 (12 Suppl 1) 13-9. SOURCE:

Journal code: COE; 8506637. ISSN: 0393-1978.

PUB. COUNTRY: Italy

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

Italian

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199408

ENTRY DATE:

Entered STN: 19940815

Last Updated on STN: 19940815 Entered Medline: 19940804

Noninvasive detection of atherosclerotic plaques AR

remains a major challenge for clinical diagnosis, therapy and prognosis. Several approaches have been explored as a tool for thrombus imaging, using platelets, antiplatelet antibodies and fibronectin or as a direct metabolic marker as low density lipoproteins or photophrine II. We tested the affinity of a new F(ab')2 monoclonal antibody (TRF1) against human fragment D-dimer of cross-linked fibrin, for atherosclerotic plaques free of

detectable thrombi on their surface. Six atherosclerotic

segments of carotid and femoral arteries, and (as a control) 5 segments

οf

atherosclerosis-free internal. . . from 11 male patients undergoing bypass surgery. All segments were carefully washed in order to dissolve and remove possible endoluminal thrombi, and were subsequently cut to obtain couples of fragments of intima of similar weight, containing

atherosclerotic plaques (n 16), or fatty streaks (n 12), or normal endothelium (n 20). Each fragment was separately put into a radioimmunoassay. . . By contrast, TRF1 binding was significantly higher (p < 0.001) in atherosclerotic than in normal fragments (26.0 \pm /-11.5% in atherosclerotic plaques, versus 9.23 +/- 9% in fatty streaks, versus 1.9 +/- 0.6% in normal endothelium.(ABSTRACT TRUNCATED AT 250 WORDS)

ANSWER 8 OF 11 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1992:443664 CAPLUS

DOCUMENT NUMBER:

117:43664

TITLE:

Polypeptides containing the fibrin-binding

domain of fibronectin, their recombinant production, and their use in imaging and therapy

Vogel, Tikva; Levanon, Avigdor; Werber, Moshe; Guy, Rachel; Panet, Amos; Hartman, Jacob; Shaked, Hadassa

PATENT ASSIGNEE(S):

Bio-Technology General Corp., USA

SOURCE:

PCT Int. Appl., 192 pp.

DOCUMENT TYPE:

CODEN: PIXXD2 Patent

LANGUAGE:

INVENTOR(S):

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE _____ -----_____ WO 9117765 A1 19911128 WO 1991-US3584 19910521

W: AU, BR, CA, FI, HU, JP, KR, NO, SU

Imaging nell'aterosclerosi: tecniche scintigrafiche.

AUTHOR: Greco C; Scopinaro F; Centi Colella A; Campa P P

CORPORATE SOURCE: II Cattedra di Cardiologia, Universita degli Studi La

Sapienza, Roma.

SOURCE: CARDIOLOGIA, (1993 Dec) 38 (12 Suppl 1) 13-9.

Journal code: COE; 8506637. ISSN: 0393-1978.

PUB. COUNTRY: Italy

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Italian

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199408

ENTRY DATE: Entered STN: 19940815

Last Updated on STN: 19940815 Entered Medline: 19940804

AB Noninvasive detection of atherosclerotic plaques

remains a major challenge for clinical diagnosis, therapy and prognosis. Several approaches have been explored as a tool for thrombus imaging, using platelets, antiplatelet antibodies and fibronectin or as a direct metabolic marker as low density lipoproteins or photophrine II. We tested the affinity of a new F(ab')2 monoclonal antibody (TRF1) against human fragment D-dimer of cross-linked fibring for athorous lengths against free of

fibrin, for atherosclerotic plaques free of

detectable thrombi on their surface. Six atherosclerotic

segments of carotid and femoral arteries, and (as a control) 5 segments

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bypass surgery. All segments were carefully washed in order to dissolve and remove possible endoluminal **thrombi**, and were subsequently cut to obtain couples of fragments of intima of similar weight, containing

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L8 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:443664 CAPLUS

DOCUMENT NUMBER: 117:43664

TITLE: Polypeptides containing the fibrin-binding

domain of fibronectin, their recombinant

production, and their use in imaging and therapy

Vogel, Tikva; Levanon, Avigdor; Werber, Moshe; Guy,

Rachel; Panet, Amos; Hartman, Jacob; Shaked, Hadassa

PATENT ASSIGNEE(S): Bio-Technology General Corp., USA

SOURCE: PCT Int. Appl., 192 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

INVENTOR(S):

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9117765 A1 19911128 WO 1991-US3584 19910521

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    HU 216302
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                      В1
                           19990818
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                      Α
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    US 6121426
                      Α
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                                                           19970811
PRIORITY APPLN. INFO.:
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                                       US 1989-345952
                                       CA 1989-2006929 A 19891229
                                                        B1 19910521
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                                       WO 1991-US3584
                                                        A 19910521
                                       US 1993-58241
                                                        A1 19930504
                                       US 1994-259569
                                                        A3 19940614
                                       US 1995-409750
                                                        A3 19950324
```

- TI Polypeptides containing the **fibrin**-binding domain of **fibronectin**, their recombinant production, and their use in imaging and therapy
- AB Polypeptides having amino acid sequences substantially present in the **fibrin**-binding domain (FBD) of human **fibronectin** are labeled with an imageable **marker** and used in imaging a **thrombus** or **atherosclerotic plaque**.

Thrombolytic agents bound to the FBD polypeptides are also claimed. Wounds are treated with fusion products of the FBD polypeptide and a polypeptide comprising the cell-binding domain of human **fibronectin**. A human **fibronectin** cDNA library was prepd. and used in cloning and making various FBD polypeptides. The polypeptides were modified with DTPA and radiolabeled with 111In and

prepd. and used in cloning and making various FBD polypeptides. The polypeptides were modified with DTPA and radiolabeled with 111In and shown

to bind to preformed thrombi and thrombi in vivo. They gave a high thrombus:blood ratio of 80-200 after 24 h. The bacterial binding domain of fibronectin was shown to be sepd. from the FBD since a 31-kDa recombinant FBD polypeptide contg. the entire FBD (residues 1-262 of fibronectin) bound to Staphylococcus aureus, while 18.5 kDa and 12 kDa polypeptides contg. the 1st 154 and 109 amino acid residues of fibronectin, resp., did not. The 18.5 and 12 kDa polypeptides had a high covalent binding specificity for fibrin together with a narrower spectrum of activities and lower specificity for other ligands such as vascular components and bacteria than the 31 kDa protein which is advantageous for thrombus imaging.

ST fibrin binding polypeptide fibronectin imaging; cloning fibronectin cDNA fibrin binding protein; thrombus imaging fibrin binding protein; atherosclerosis plaque imaging

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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
    US 5270030
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                       B2
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                      Α
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                                           US 1995-409750
                                                            19950324
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                            19990209
                                           US 1997-826885
                      Α
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                                           US 1997-909140
    US 6121426
                      Α
                            20000919
                                                            19970811
                                        US 1990-526397 A 19900521
PRIORITY APPLN. INFO.:
                                        US 1988-291951
                                                         B2 19881229
                                                         B2 19890428
                                        US 1989-345952
                                        CA 1989-2006929 A 19891229
                                                         B1 19910521
                                        US 1991-703842
                                        WO 1991-US3584
                                                         A 19910521
                                        US 1993-58241
                                                         A1 19930504
                                        US 1994-259569
                                                         A3 19940614
                                        US 1995-409750
                                                         A3 19950324
```

- TI Polypeptides containing the **fibrin**-binding domain of **fibronectin**, their recombinant production, and their use in imaging and therapy
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Thrombolytic agents bound to the FBD polypeptides are also claimed. Wounds are treated with fusion products of the FBD polypeptide and a polypeptide comprising the cell-binding domain of human

fibronectin. A human fibronectin cDNA library was

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to bind to preformed thrombi and thrombi in vivo. They gave a high thrombus:blood ratio of 80-200 after 24 h. The bacterial binding domain of fibronectin was shown to be sepd. from the FBD since a 31-kDa recombinant FBD polypeptide contg. the entire FBD (residues 1-262 of fibronectin) bound to Staphylococcus aureus, while 18.5 kDa and 12 kDa polypeptides contg. the 1st 154 and 109 amino acid residues of fibronectin, resp., did not. The 18.5 and 12 kDa polypeptides had a high covalent binding specificity for fibrin together with a narrower spectrum of activities and lower specificity for other ligands such as vascular components and bacteria than the 31 kDa protein which is advantageous for thrombus imaging.

ST fibrin binding polypeptide fibronectin imaging; cloning fibronectin cDNA fibrin binding protein; thrombus imaging fibrin binding protein; atherosclerosis plaque imaging

```
IT
     Bacteria
     Cell
     Escherichia coli
        (DNA for fibrin-binding polypeptide of human
        fibronectin cloning and expression in)
IT
     Plasmid and Episome
        (DNA for fibrin-binding polypeptides of human
        fibronectin on, cloning and expression of)
TΤ
     Gene, animal
     RL: BIOL (Biological study)
        (cDNA, for fibrin-binding polypeptides of human
        fibronectin, cloning and expression in Escherichia coli of)
IT
     Blood vessel, composition
        (components of, recombinant fibrin-binding polypeptides of
        human fibronectin response to)
IT
     Thrombolytics
        (conjugates with fibrin-binding polypeptides of human
        fibronectin)
TΥ
     Fibrins
     RL: BIOL (Biological study)
        (domain of human fibronectin binding to, labeled polypeptides
        contg., for imaging)
IT
     Wound healing promoters
        (fibrin-binding polypeptides of human fibronectin
        and cell-binding polypeptides of fibronectin as)
IT
     Fibronectins
     RL: BIOL (Biological study)
        (fibrin-binding polypeptides of, labeled, for imaging)
     Deoxyribonucleic acids
TΤ
     RL: BIOL (Biological study)
        (for fibrin-binding polypeptides of human fibronectin
        , cloning and expression of)
ΙT
     Anticoagulants and Antithrombotics
        (fusion proteins contg. fibrin-binding polypeptides of human
        fibronectin as)
IT
     Thrombus and Blood clot
        (imaging of, with labeled fibrin-binding polypeptides of
        human fibronectin)
IT
     Imaging
        (labeled fibrin-binding polypeptides of fibronectin
        for)
IT
     Molecular cloning
        (of DNA for fibrin-binding polypeptides of human
        fibronectin on)
ΙT
     Plasmid and Episome
        (pFN194-2, DNA for fusion protein contg. fibrin-binding and
        cell-binding polypeptides of human fibronectin on, cloning
        and expression of)
IT
     Plasmid and Episome
        (pFN195-4, DNA for fusion protein contg. fibrin-binding
        polypeptide of human fibronectin on, cloning and expression
        of)
     Plasmid and Episome
IT
        (pFN196-2, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
ΙT
     Plasmid and Episome
        (pFN197-10, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
```

```
ΙT
     Bacteria
     Cell
     Escherichia coli
        (DNA for fibrin-binding polypeptide of human
        fibronectin cloning and expression in)
     Plasmid and Episome
IT
        (DNA for fibrin-binding polypeptides of human
        fibronectin on, cloning and expression of)
IT
     Gene, animal
     RL: BIOL (Biological study)
        (cDNA, for fibrin-binding polypeptides of human
        fibronectin, cloning and expression in Escherichia coli of)
TT
     Blood vessel, composition
        (components of, recombinant fibrin-binding polypeptides of
        human fibronectin response to)
IT
     Thrombolytics
        (conjugates with fibrin-binding polypeptides of human
        fibronectin)
IT
     Fibrins
     RL: BIOL (Biological study)
        (domain of human fibronectin binding to, labeled polypeptides
        contg., for imaging)
IT
     Wound healing promoters
        (fibrin-binding polypeptides of human fibronectin
        and cell-binding polypeptides of fibronectin as)
IT
     Fibronectins
     RL: BIOL (Biological study)
        (fibrin-binding polypeptides of, labeled, for imaging)
IT
     Deoxyribonucleic acids
     RL: BIOL (Biological study)
        (for fibrin-binding polypeptides of human fibronectin
        , cloning and expression of)
     Anticoagulants and Antithrombotics
IT
        (fusion proteins contg. fibrin-binding polypeptides of human
        fibronectin as)
     Thrombus and Blood clot
IT
        (imaging of, with labeled fibrin-binding polypeptides of
        human fibronectin)
IT
     Imaging
        (labeled fibrin-binding polypeptides of fibronectin
        for)
IT
     Molecular cloning
        (of DNA for fibrin-binding polypeptides of human
        fibronectin on)
IT
     Plasmid and Episome
        (pFN194-2, DNA for fusion protein contg. fibrin-binding and
        cell-binding polypeptides of human fibronectin on, cloning
        and expression of)
IT
     Plasmid and Episome
        (pFN195-4, DNA for fusion protein contg. fibrin-binding
        polypeptide of human fibronectin on, cloning and expression
        of)
IT
     Plasmid and Episome
        (pFN196-2, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
IT
     Plasmid and Episome
        (pFN197-10, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
```

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ΤТ
     Plasmid and Episome
        (pFN202-5, DNA for fusion protein contg. fibrin-binding and
        cell-binding polypeptides of human fibronectin on, cloning
        and expression of)
ΙT
     Plasmid and Episome
        (pFN203-2, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
IT
     Plasmid and Episome
        (pFN205-5, DNA for fusion protein contg. fibrin-binding
        polypeptide of human fibronectin on, cloning and expression
        in Escherichia coli of)
     Plasmid and Episome
ΙT
        (pFN208-13, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
TΤ
     Plasmid and Episome
        (pFN962-3, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
IT
     Extracellular matrix
     Staphylococcus aureus
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding response to)
IT
     Eye, disease
        (wound, treatment of, with fibrin-binding and cell-binding
        polypeptides of human fibronectin)
IT
     Endothelium
        (Staphylococcus aureus binding to cells of, recombinant fibrin
        -binding polypeptides of human fibronectin effect on)
IT
     Imaging
        (NMR, agents, paramagnetic ion conjugates with fibrin-binding
        polypeptides of human fibronectin as)
ΙT
     Arteriosclerosis
        (atherosclerosis, plaque, imaging of, with labeled fibrin
        -binding polypeptides of human fibronectin)
IT
     Deoxyribonucleic acids
     RL: BIOL (Biological study)
        (complementary, for fibrin-binding polypeptides of human
        fibronectin, cloning and expression in Escherichia coli of)
IT
     Fibrins
     RL: PROC (Process)
        (complexes, with recombinant fibrin-binding polypeptides of
        human fibronectin, characterization of)
IT
     Radioelements, compounds
     RL: BIOL (Biological study)
        (conjugates, with fibrin-binding polypeptides of human
        fibronectin, for imaging)
IT
     Scintigraphy
        (contrast agents, radioactive isotope conjugates with
        fibrin-binding polypeptides of human fibronectin as)
IT
     Radiography
        (contrast agents, x-ray-opaque element conjugates with fibrin
        -binding polypeptides of human fibronectin as)
IT
        (cornea, epithelium, wound, treatment of, with fibrin-binding
        and cell-binding polypeptides of human fibronectin)
IT
    Eve
        (cornea, stroma, wound, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
```

```
IT
     Plasmid and Episome
        (pFN202-5, DNA for fusion protein contg. fibrin-binding and
        cell-binding polypeptides of human fibronectin on, cloning
        and expression of)
IT
     Plasmid and Episome
        (pFN203-2, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
     Plasmid and Episome
IT
        (pFN205-5, DNA for fusion protein contg. fibrin-binding
        polypeptide of human fibronectin on, cloning and expression
        in Escherichia coli of)
     Plasmid and Episome
ΙT
        (pFN208-13, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
IT
     Plasmid and Episome
        (pFN962-3, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
     Extracellular matrix
ΤТ
     Staphylococcus aureus
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding response to)
ΙT
     Eye, disease
        (wound, treatment of, with fibrin-binding and cell-binding
        polypeptides of human fibronectin)
IT
     Endothelium
        (Staphylococcus aureus binding to cells of, recombinant fibrin
        -binding polypeptides of human fibronectin effect on)
TT
     Imaging
        (NMR, agents, paramagnetic ion conjugates with fibrin-binding
        polypeptides of human fibronectin as)
ΙT
     Arteriosclerosis
        (atherosclerosis, plaque, imaging of, with labeled fibrin
        -binding polypeptides of human fibronectin)
IT
     Deoxyribonucleic acids
     RL: BIOL (Biological study)
        (complementary, for fibrin-binding polypeptides of human
        fibronectin, cloning and expression in Escherichia coli of)
IT
     Fibrins
     RL: PROC (Process)
        (complexes, with recombinant fibrin-binding polypeptides of
        human fibronectin, characterization of)
IT
     Radioelements, compounds
     RL: BIOL (Biological study)
        (conjugates, with {\tt fibrin}{\tt -}{\tt binding} polypeptides of human
        fibronectin, for imaging)
IT
     Scintigraphy
        (contrast agents, radioactive isotope conjugates with
        fibrin-binding polypeptides of human fibronectin as)
IT
     Radiography
        (contrast agents, x-ray-opaque element conjugates with fibrin
        -binding polypeptides of human fibronectin as)
IT
        (cornea, epithelium, wound, treatment of, with fibrin-binding
        and cell-binding polypeptides of human fibronectin)
IT
     Eye
        (cornea, stroma, wound, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
```

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IT
     Tendon
        (disease, injury, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
     Proteins, specific or class
IT
     RL: BIOL (Biological study)
        (fibrin-binding, labeled, of human fibronectin, for
        imaging agents)
IT
     Proteins, specific or class
     RL: BIOL (Biological study)
        (fusion products, of cell-binding domain and fibrin-binding
        domain polypeptides of human fibronectin)
IT
     Plasmid and Episome
        (pFN949-2, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
     Plasmid and Episome
ΙT
        (pFN975-25, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
     Magnetic substances
IT
        (para-, conjugates with fibrin-binding polypeptides of human
        fibronectin, for imaging)
TΤ
     Skin
        (transplant, wound in, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
ΙT
     Opaque materials
        (x-ray, conjugates with fibrin-binding polypeptides of human
        fibronectin, for imaging)
TΤ
     67-43-6D, DTPA, reaction products with recombinant fibrin
     -binding polypeptides of human fibronectin, indium-111-labeled
     142298-13-3D, DTPA reaction products, indium-111-labeled
                                                                142298-17-7D,
     DTPA reaction products, indium-111-labeled, recombinant deriv.
     142298-19-9D, DTPA reaction products, indium-111-labeled
                                                                142298-20-2D,
     DTPA reaction products, indium-111-labeled
     RL: BIOL (Biological study)
        (atherosclerotic lesions and thrombi imaging with)
ΙT
     142298-11-1
     RL: BIOL (Biological study)
        (cloning of cDNA for, in recombinant fibrin-binding
        polypeptides prepn. for imaging agents)
IT
     142244-17-5
                 142244-18-6
     RL: PROC (Process)
        (cloning of, in recombinant fibrin-binding polypeptides
        prepn. for imaging agents)
IT
     10043-66-0D, Iodine-131, fibrin-binding polypeptide conjugates
     14119-09-6D, Gallium-67, fibrin-binding polypeptide conjugates
     14158-31-7D, Iodine-125, fibrin-binding polypeptide conjugates
     14932-42-4D, Xenon-133, fibrin-binding polypeptide conjugates
     15715-08-9D, Iodine-123, fibrin-binding polypeptide conjugates
     15750-15-9D, Indium-111, fibrin-binding polypeptide conjugates
     141517-93-3D, fusion product with fibrin-binding polypeptides of
     human fibronectin
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for imaging)
     142298-12-2, 1-109-Fibronectin (human clone pFH16/pFH134 protein
IT
     moiety reduced) 142298-16-6, 1-153-Fibronectin (human clone
     pFH16/pFH134 protein moiety reduced)
                                           142298-17-7
                                                         142298-18-8, 1-154-
     Fibronectin (human clone pFH16/pFH134 protein moiety reduced)
     RL: BIOL (Biological study)
        (for imaging agent)
```

```
ΙT
     Tendon
        (disease, injury, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
     Proteins, specific or class
IT
     RL: BIOL (Biological study)
        (fibrin-binding, labeled, of human fibronectin, for
        imaging agents)
IT
     Proteins, specific or class
     RL: BIOL (Biological study)
        (fusion products, of cell-binding domain and fibrin-binding
        domain polypeptides of human fibronectin)
IT
     Plasmid and Episome
        (pFN949-2, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
     Plasmid and Episome
IT
        (pFN975-25, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
     Magnetic substances
ТТ
        (para-, conjugates with fibrin-binding polypeptides of human
        fibronectin, for imaging)
TΨ
     Skin
        (transplant, wound in, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
IT
     Opaque materials
        (x-ray, conjugates with fibrin-binding polypeptides of human
        fibronectin, for imaging)
ΙT
     67-43-6D, DTPA, reaction products with recombinant fibrin
     -binding polypeptides of human fibronectin, indium-111-labeled
     142298-13-3D, DTPA reaction products, indium-111-labeled
                                                                 142298-17-7D,
     DTPA reaction products, indium-111-labeled, recombinant deriv.
     142298-19-9D, DTPA reaction products, indium-111-labeled
                                                                142298-20-2D,
     DTPA reaction products, indium-111-labeled
     RL: BIOL (Biological study)
        (atherosclerotic lesions and thrombi imaging with)
IT
     142298-11-1
     RL: BIOL (Biological study)
        (cloning of cDNA for, in recombinant fibrin-binding
        polypeptides prepn. for imaging agents)
IT
     142244-17-5
                 142244-18-6
     RL: PROC (Process)
        (cloning of, in recombinant fibrin-binding polypeptides
        prepn. for imaging agents)
     10043-66-0D, Iodine-131, fibrin-binding polypeptide conjugates
IT
     14119-09-6D, Gallium-67, fibrin-binding polypeptide conjugates
     14158-31-7D, Iodine-125, fibrin-binding polypeptide conjugates
     14932-42-4D, Xenon-133, fibrin-binding polypeptide conjugates
     15715-08-9D, Iodine-123, fibrin-binding polypeptide conjugates
     15750-15-9D, Indium-111, fibrin-binding polypeptide conjugates
     141517-93-3D, fusion product with fibrin-binding polypeptides of
     human fibronectin
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for imaging)
TΤ
     142298-12-2, 1-109-Fibronectin (human clone pFH16/pFH134 protein
                     142298-16-6, 1-153-Fibronectin (human clone
     moiety reduced)
                                            142298-17-7
     pFH16/pFH134 protein moiety reduced)
                                                         142298-18-8, 1-154-
     Fibronectin (human clone pFH16/pFH134 protein moiety reduced)
     RL: BIOL (Biological study)
        (for imaging agent)
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14133-76-7D, Technetium-99, fibrin-binding polypeptide
     conjugates 15678-91-8D, fibrin-binding polypeptide conjugates,
     biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for imaging, metastable)
     141497-06-5
                 141497-07-6
ΙT
     RL: PRP (Properties)
        (imageable marker-labeled fibrin-binding
        polypeptides of fibronectin contg. amino-terminal sequence
        of, for imaging agents)
TΤ
     68181-17-9DP, N-Succinimidyl-3-(2-pyridyldithio)propionate, reaction
     products with recombinant fibrin-binding polypeptides of human
     fibronectin and thiolated streptokinase
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of and biol. activity of)
ΙT
     80146-85-6, Transglutaminase
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding to fibrin clot in response to)
     9005-49-6, Heparin, biological studies
IT
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding to fibrin clots response to)
     9005-49-6D, Heparin, Sepharose conjugates 9012-36-6D, Sepharose,
ΙT
heparin
     conjugates
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin purifn. with)
TΤ
     9001-92-7D, Protease, conjugates with fibrin-binding
     polypeptides of human fibronectin 9002-01-1D, Streptokinase,
     conjugates with fibrin-binding polypeptides of human
                   9039-53-6D, Urokinase, conjugates with
     fibronectin
     fibrin-binding polypeptides of human fibronectin
     81669-57-0D, Anistreplase, conjugates with fibrin-binding
     polypeptides of human fibronectin
                                        82657-92-9D, Prourokinase,
     conjugates with fibrin-binding polypeptides of human
     fibronectin
                  139639-23-9D, conjugates with fibrin
     -binding polypeptides of human fibronectin
     RL: BIOL (Biological study)
        (thrombus treatment with)
     ANSWER 9 OF 11
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                    88274546
ACCESSION NUMBER:
                                 MEDLINE
DOCUMENT NUMBER:
                    88274546
                               PubMed ID: 3392585
TITLE:
                    Iodine-131-labeled fibronectin: potential agent
                    for imaging atherosclerotic lesion and thrombus.
AUTHOR:
                    Uehara A; Isaka Y; Hashikawa K; Kimura K; Kozuka T; Kamada
                    T; Etani H; Yoneda S; Imaizumi M
CORPORATE SOURCE:
                    First Department of Internal Medicine, Osaka University
                    Medical School, Japan.
                    JOURNAL OF NUCLEAR MEDICINE, (1988 Jul) 29 (7) 1264-7.
SOURCE:
                    Journal code: JEC; 0217410. ISSN: 0161-5505.
PUB. COUNTRY:
                    United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:
                    English
FILE SEGMENT:
                    Priority Journals
ENTRY MONTH:
                    198808
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IT
     14133-76-7D, Technetium-99, fibrin-binding polypeptide
     conjugates 15678-91-8D, fibrin-binding polypeptide conjugates,
     biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for imaging, metastable)
ΙT
     141497-06-5
                 141497-07-6
     RL: PRP (Properties)
        (imageable marker-labeled fibrin-binding
        polypeptides of fibronectin contg. amino-terminal sequence
        of, for imaging agents)
ΤT
     68181-17-9DP, N-Succinimidyl-3-(2-pyridyldithio)propionate, reaction
     products with recombinant fibrin-binding polypeptides of human
     fibronectin and thiolated streptokinase
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of and biol. activity of)
IT
     80146-85-6, Transglutaminase
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding to fibrin clot in response to)
     9005-49-6, Heparin, biological studies
TT
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding to fibrin clots response to)
     9005-49-6D, Heparin, Sepharose conjugates 9012-36-6D, Sepharose,
ΙT
heparin
     conjugates
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin purifn. with)
IT
     9001-92-7D, Protease, conjugates with fibrin-binding
     polypeptides of human fibronectin 9002-01-1D, Streptokinase,
     conjugates with fibrin-binding polypeptides of human
                   9039-53-6D, Urokinase, conjugates with
     fibronectin
     fibrin-binding polypeptides of human fibronectin
     81669-57-0D, Anistreplase, conjugates with fibrin-binding
     polypeptides of human fibronectin
                                       82657-92-9D, Prourokinase,
     conjugates with fibrin-binding polypeptides of human
     fibronectin
                  139639-23-9D, conjugates with fibrin
     -binding polypeptides of human fibronectin
     RL: BIOL (Biological study)
        (thrombus treatment with)
    ANSWER 9 OF 11
                        MEDLINE
                    88274546
ACCESSION NUMBER:
                                 MEDLINE
                               PubMed ID: 3392585
DOCUMENT NUMBER:
                    88274546
TITLE:
                    Iodine-131-labeled fibronectin: potential agent
                    for imaging atherosclerotic lesion and thrombus.
AUTHOR:
                    Uehara A; Isaka Y; Hashikawa K; Kimura K; Kozuka T; Kamada
                    T; Etani H; Yoneda S; Imaizumi M
CORPORATE SOURCE:
                    First Department of Internal Medicine, Osaka University
                    Medical School, Japan.
                    JOURNAL OF NUCLEAR MEDICINE, (1988 Jul) 29 (7) 1264-7.
SOURCE:
                    Journal code: JEC; 0217410. ISSN: 0161-5505.
PUB. COUNTRY:
                    United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:
                    English
FILE SEGMENT:
                   Priority Journals
```

ENTRY MONTH:

198808

ENTRY DATE: Entered STN: 19900308 Last Updated on STN: 19900308 Entered Medline: 19880819 Iodine-131-labeled fibronectin: potential agent for imaging TIatherosclerotic lesion and thrombus. Fibronectin is known to interact with fibrin, AB collagen, etc. We have labeled fibronectin with 131I, and measured its accumulation in the deendothelialized lesion in the rabbit aorta to evaluate it as a candidate for imaging atherosclerotic lesions and thrombi. Accumulation of [131I] fibronectin in the deendothelialized lesion was apparent at $48\ \mathrm{hr}$, and increased at $72\ \mathrm{hr}$ after injection of the agent. Our results indicate that radiolabeled fibronectin may be a useful tracer for imaging early atherosclerotic lesion and thrombus. CT Check Tags: Animal; Male *Arteriosclerosis: RI, radionuclide imaging *Fibronectins: DU, diagnostic use *Iodine Radioisotopes: DU, diagnostic use Isotope Labeling: MT, methods Rabbits *Thrombosis: RI, radionuclide imaging CN 0 (Fibronectins); 0 (Iodine Radioisotopes) ANSWER 10 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 3 82154437 EMBASE ACCESSION NUMBER: DOCUMENT NUMBER: 1982154437 TITLE: [Distribution of fibronectin in renal pathology]. DISTRIBUTION DE LA FIBRONECTINE EN PATHOLOGIE RENALE. Birembaut P.; Gaillard D.; Labat-Robert J.; Robert L. AUTHOR: Lab. Pol Bouin, CHU, 51100 Reims, France Nephrologie, (1982) 3/1 (23-26). CORPORATE SOURCE: SOURCE: CODEN: NEPHDY Switzerland COUNTRY: DOCUMENT TYPE: Journal Urology and Nephrology FILE SEGMENT: 028 005 General Pathology and Pathological Anatomy LANGUAGE: French SUMMARY LANGUAGE: English [Distribution of fibronectin in renal pathology]. DISTRIBUTION DE LA FIBRONECTINE EN PATHOLOGIE RENALE. The distribution of fibronectin (FN), a major glycoproteic AΒ component of extracellular matrix, has been detected in the human kidney by an indirect immunofluorescence technique. . . of glomeruli. In glomerulonephritis with endo- and/or extracapillary proliferation, FN was increased around messangial cells. FN was also bound to fibrin in epithelial crescents, fibrinoid necrosis and in thrombi of thrombotic microangiopathy. FN was increased in the mesangium of diabetic glomeruli without endocappillary proliferation. FN has not been found in amyloid deposits and in sclerosed glomeruli. We therefore conclude that FN is a good mesangial marker and is probably involved in the inflammatory process. CT Medical Descriptors: *inflammation *kidney disease

*mesangium kidney histology ENTRY DATE:

Entered STN: 19900308

Last Updated on STN: 19900308 Entered Medline: 19880819

ΤI Iodine-131-labeled fibronectin: potential agent for imaging atherosclerotic lesion and thrombus.

Fibronectin is known to interact with fibrin, AΒ collagen, etc. We have labeled fibronectin with 131I, and measured its accumulation in the deendothelialized lesion in the rabbit aorta to evaluate it as a candidate for imaging atherosclerotic lesions and thrombi. Accumulation of [131I] fibronectin in the deendothelialized lesion was apparent at 48 hr, and increased at 72 hr after injection of the agent. Our results indicate that radiolabeled fibronectin may be a useful tracer for imaging early

Check Tags: Animal; Male

*Arteriosclerosis: RI, radionuclide imaging

*Fibronectins: DU, diagnostic use

atherosclerotic lesion and thrombus.

*Iodine Radioisotopes: DU, diagnostic use

Isotope Labeling: MT, methods

Rabbits

*Thrombosis: RI, radionuclide imaging 0 (Fibronectins); 0 (Iodine Radioisotopes)

ANSWER 10 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V. DUPLICATE 3

ACCESSION NUMBER:

82154437 EMBASE

DOCUMENT NUMBER:

1982154437

TITLE:

CN

[Distribution of fibronectin in renal pathology].

DISTRIBUTION DE LA FIBRONECTINE EN PATHOLOGIE RENALE. Birembaut P.; Gaillard D.; Labat-Robert J.; Robert L.

AUTHOR: CORPORATE SOURCE:

Lab. Pol Bouin, CHU, 51100 Reims, France

SOURCE:

Nephrologie, (1982) 3/1 (23-26).

CODEN: NEPHDY

COUNTRY:

Switzerland

DOCUMENT TYPE:

Journal

FILE SEGMENT:

028 Urology and Nephrology

General Pathology and Pathological Anatomy 005

LANGUAGE:

French SUMMARY LANGUAGE: English

[Distribution of fibronectin in renal pathology]. DISTRIBUTION DE LA FIBRONECTINE EN PATHOLOGIE RENALE.

AΒ The distribution of fibronectin (FN), a major glycoproteic component of extracellular matrix, has been detected in the human kidney by an indirect immunofluorescence technique. . . of glomeruli. In glomerulonephritis with endo- and/or extracapillary proliferation, FN was increased around messangial cells. FN was also bound to fibrin in epithelial crescents, fibrinoid necrosis and in thrombi of thrombotic microangiopathy. FN was increased in the mesangium of diabetic glomeruli without endocappillary proliferation. FN has not been found in amyloid deposits and in sclerosed glomeruli. We therefore conclude that

FN

is a good mesangial marker and is probably involved in the inflammatory process.

CTMedical Descriptors:

*inflammation

*kidney disease

*mesangium

kidney

histology

*fibronectin

(fibronectin) 86088-83-7 RN

ANSWER 11 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS

1982:307656 BIOSIS ACCESSION NUMBER:

DOCUMENT NUMBER:

BA74:80136

TITLE: AUTHOR(S):

DISTRIBUTION OF FIBRONECTIN IN RENAL PATHOLOGY. BIREMBAUT P; GAILLARD D; LABAT-ROBERT J; ROBERT L LAB. POL BOUIN, CENT. HOSP. UNIV., 51100 REIMS.

CORPORATE SOURCE:

NEPHROLOGIE, (1902) 3 (1), 23-26.

CODEN: NEPHDY. ISSN: 0250-4960.

FILE SEGMENT:

BA; OLD

LANGUAGE:

French

ΤI DISTRIBUTION OF FIBRONECTIN IN RENAL PATHOLOGY.

The distribution of fibronectin (FN), a major glycoproteic component of extracellular matrix, was detected in the human kidney by an indirect immunofluorescence technique using. . . of glomeruli. In glomerulonephritis with endo and/or extracapillary proliferation, FN was increased around mesangial cells. FN was also bound to fibrin in epithelial crescents, fibrinoid necrosis and in thrombi of

thrombotic microangiopathy. FN was increased in the mesangium of diabetic glomeruli without endocapillary proliferation. FN was not found in

amyloid

deposits and in sclerosed glomeruli. Apparently, FN is a good mesangial marker and is probably involved in the inflammatory process.

=> dis L9 1-9 ibib kwic

ANSWER 1 OF 9 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1

ACCESSION NUMBER:

2001142593 EMBASE

TITLE:

Radiolabeled peptides in the detection of deep venous

thrombosis.

AUTHOR:

Taillefer R.

CORPORATE SOURCE:

Dr. R. Taillefer, Department of Nuclear Medicine,

Hotel-Dieu de Montreal, 3840 rue St-Urbain, Montreal, H2W

1T8, Canada

SOURCE:

Seminars in Nuclear Medicine, (2001) 31/2 (102-123).

Refs: 55

ISSN: 0001-2998 CODEN: SMNMAB

COUNTRY:

United States

DOCUMENT TYPE: FILE SEGMENT:

Journal; General Review 023 Nuclear Medicine 037 Drug Literature Index

LANGUAGE:

English

SUMMARY LANGUAGE: English

. . . by various disease-related and technical factors. An alternative approach to the diagnosis of acute DVT is to detect a molecular

marker of acute DVT that is not present in old, organized DVT. Recent advances in biotechnology permit the use of highly specific synthetic peptide or small molecular markers, which are involved in the acute stages of DVT formation and can be labeled efficiently with (99m)Tc. (99m)Tc-apcitide, a glycoprotein. . . acute DVT. Two other agents are currently under clinical investigation: (99m)Tc-DMP 444, which is another GP IIb/IIIa receptor antagonist, and (99m)Tc-Fibrin-

Binding Domain (FBD), a radio-labeled fibrin-

binding domain of fibronectin. Different

clinical studies have shown a high diagnostic accuracy with these

*fibronectin

RN (fibronectin) 86088-83-7

L8 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1982:307656 BIOSIS

DOCUMENT NUMBER: BA74:80136

TITLE: DISTRIBUTION OF FIBRONECTIN IN RENAL PATHOLOGY.

AUTHOR(S): BIREMBAUT P; GAILLARD D; LABAT-ROBERT J; ROBERT L

CORPORATE SOURCE: LAB. POL BOUIN, CENT. HOSP. UNIV., 51100 REIMS.

SOURCE: NEPHROLOGIE, (1902) 3 (1), 23-26.

CODEN: NEPHDY. ISSN: 0250-4960.

FILE SEGMENT: BA; OLD LANGUAGE: French

TI DISTRIBUTION OF FIBRONECTIN IN RENAL PATHOLOGY.

AB The distribution of **fibronectin** (FN), a major glycoproteic component of extracellular matrix, was detected in the human kidney by an indirect immunofluorescence technique using. . . of glomeruli. In glomerulonephritis with endo and/or extracapillary proliferation, FN was increased around mesangial cells. FN was also bound to **fibrin** in epithelial crescents, fibrinoid necrosis and in **thrombi** of

thrombotic microangiopathy. FN was increased in the mesangium of diabetic glomeruli without endocapillary proliferation. FN was not found in

amyloid

deposits and in sclerosed glomeruli. Apparently, FN is a good mesangial marker and is probably involved in the inflammatory process.

=> dis L9 1-9 ibib kwic

L9 ANSWER 1 OF 9 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1

ACCESSION NUMBER: 2001142593 EMBASE

TITLE: Radiolabeled peptides in the detection of deep venous

thrombosis.

AUTHOR: Taillefer R.

CORPORATE SOURCE: Dr. R. Taillefer, Department of Nuclear Medicine,

Hotel-Dieu de Montreal, 3840 rue St-Urbain, Montreal, H2W

1T8, Canada

SOURCE: Seminars in Nuclear Medicine, (2001) 31/2 (102-123).

Refs: 55

ISSN: 0001-2998 CODEN: SMNMAB

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 023 Nuclear Medicine
037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

AB . . . by various disease-related and technical factors. An alternative approach to the diagnosis of acute DVT is to detect a molecular marker of acute DVT that is not present in old, organized DVT.

Recent advances in biotechnology permit the use of highly specific synthetic peptide or small molecular markers, which are involved in the acute stages of DVT formation and can be labeled efficiently with (99m)Tc. (99m)Tc-apcitide, a glycoprotein. . . acute DVT. Two other agents are currently under clinical investigation: (99m)Tc-DMP 444, which is another GP IIb/IIIa receptor antagonist, and (99m)Tc-Fibrin-

Binding Domain (FBD), a radio-labeled fibrin-

binding domain of fibronectin. Different

clinical studies have shown a high diagnostic accuracy with these

```
synthetic (99m)Tc-labeled peptides in the detection of acute DVT..
CT
    Medical Descriptors:
     *deep vein thrombosis: DI, diagnosis
     *protein analysis
       isotope labeling
     peptide analysis
     diagnostic value
     reliability
     color ultrasound flowmetry
     biotechnology
     drug mechanism
     human
    human tissue
    human cell
     review
       *fibronectin: EC, endogenous compound
     *fibrinogen receptor antagonist: PD, pharmacology
     *technetium 99m
     (fibronectin) 86088-83-7; (technetium 99m) 14133-76-7
RN
    ANSWER 2 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS
L9
                    2001:225518 BIOSIS
ACCESSION NUMBER:
                    PREV200100225518
DOCUMENT NUMBER:
TITLE:
                    Fibrin binding domain
                    polypeptides and uses and methods of producing same.
                    Vogel, Tikv (1); Levanon, Avigdor; Werber, Moshe; Guy,
AUTHOR(S):
                    Rachel; Panet, Amos
CORPORATE SOURCE:
                    (1) Rehovot Israel
                    ASSIGNEE: Bio-Technology General Corp.
PATENT INFORMATION: US 6121426 September 19, 2000
                    Official Gazette of the United States Patent and Trademark
SOURCE:
                    Office Patents, (Sep. 19, 2000) Vol. 1238, No. 3, pp. No
                    Pagination. e-file.
                    ISSN: 0098-1133.
DOCUMENT TYPE:
                    Patent
LANGUAGE:
                    English
     Fibrin binding domain polypeptides and uses
     and methods of producing same.
     This invention provides an imaging agent which comprises a polypeptide
AB
     labeled with an imageable marker, such polypeptide having an
     amino acid sequence substantially present in the fibrin
     binding domain of naturally-occurring human
     fibronectin and being capable of binding to fibrin. The
     invention further provides a method wherein the imaging agent is used for
     imaging a fibrin-containing substance, i.e., a thrombus or
     atherosclerotic plaque. Further provided are plasmids for expression of
     polypeptides having an amino acid sequence substantially present in the
     fibrin binding domain of naturally-occurring
     human fibronectin and being capable of binding to fibrin
     , hosts containing these plasmids, methods of producing the polypeptides,
     methods of treatment using the polypeptides, and methods of recovering,
     refolding. . . purified polypeptides substantially free of other
     substances of human origin which have an amino acid sequence
substantially
     present in the fibrin binding domain of
     naturally-occurring human fibronectin and which are capable of
     binding to fibrin.
```

```
CT
    Medical Descriptors:
     *deep vein thrombosis: DI, diagnosis
     *protein analysis
       isotope labeling
     peptide analysis
     diagnostic value
     reliability
     color ultrasound flowmetry
     biotechnology
     drug mechanism
     human
     human tissue
     human cell
     review
       *fibronectin: EC, endogenous compound
     *fibrinogen receptor antagonist: PD, pharmacology
     *technetium 99m
     (fibronectin) 86088-83-7; (technetium 99m) 14133-76-7
RN
    ANSWER 2 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS
T.9
                    2001:225518 BIOSIS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                    PREV200100225518
TITLE:
                    Fibrin binding domain
                    polypeptides and uses and methods of producing same.
                    Vogel, Tikv (1); Levanon, Avigdor; Werber, Moshe; Guy,
AUTHOR(S):
                    Rachel; Panet, Amos
CORPORATE SOURCE:
                   (1) Rehovot Israel
                    ASSIGNEE: Bio-Technology General Corp.
PATENT INFORMATION: US 6121426 September 19, 2000
SOURCE:
                    Official Gazette of the United States Patent and Trademark
                    Office Patents, (Sep. 19, 2000) Vol. 1238, No. 3, pp. No
                    Pagination. e-file.
                    ISSN: 0098-1133.
DOCUMENT TYPE:
                    Patent
LANGUAGE:
                    English
     Fibrin binding domain polypeptides and uses
     and methods of producing same.
     This invention provides an imaging agent which comprises a polypeptide
AB
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     amino acid sequence substantially present in the fibrin
     binding domain of naturally-occurring human
     fibronectin and being capable of binding to fibrin. The
     invention further provides a method wherein the imaging agent is used for
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     atherosclerotic plaque. Further provided are plasmids for expression of
     polypeptides having an amino acid sequence substantially present in the
     fibrin binding domain of naturally-occurring
     human fibronectin and being capable of binding to fibrin
     , hosts containing these plasmids, methods of producing the polypeptides,
     methods of treatment using the polypeptides, and methods of recovering,
     refolding. . . purified polypeptides substantially free of other
     substances of human origin which have an amino acid sequence
substantially
     present in the fibrin binding domain of
     naturally-occurring human fibronectin and which are capable of
     binding to fibrin.
```

synthetic (99m)Tc-labeled peptides in the detection of acute DVT.. . .

IT Major Concepts

Biochemistry and Molecular Biophysics; Radiology (Medical Sciences)

ΙT Chemicals & Biochemicals

fibrin binding domain polypeptides:

imaging agents

IT Miscellaneous Descriptors

fibrin-containing domain

L9ANSWER 3 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: DOCUMENT NUMBER:

2000:277499 BIOSIS PREV200000277499

TITLE:

Fibrin binding domain

polypeptides and uses and methods of producing same. Vogel, Tikv (1); Levanon, Avigdor; Werber, Moshe; Guy,

AUTHOR(S):

Rachel; Panet, Amos

CORPORATE SOURCE:

(1) Rehovot Israel

ASSIGNEE: Bio-Technology General Corp., Iselin, NJ, USA

PATENT INFORMATION: US 5965383 October 12, 1999

SOURCE:

Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 12, 1999) Vol. 1227, No. 2, pp. No

pagination. e-file.. ISSN: 0098-1133.

DOCUMENT TYPE:

Patent English

LANGUAGE:

Fibrin binding domain polypeptides and uses

and methods of producing same.

This invention provides an imaging agent which comprises a polypeptide AB

labeled with an imageable marker, such polypeptide having an

amino acid sequence substantially present in the fibrin

binding domain of naturally-occurring human

fibronectin and being capable of binding to fibrin. The

invention further provides a method wherein the imaging agent is used for

imaging a fibrin-containing substance, i.e., a thrombus-or

atherosclerotic plaque. Further provided are plasmids for expression of polypeptides having an amino acid sequence substantially present in the

fibrin binding domain of naturally-occurring

human fibronectin and being capable of binding to fibrin

, hosts containing these plasmids, methods of producing the polypeptides, methods of treatment using the polypeptides, and methods of recovering, . . purified polypeptides substantially free of other refolding.

substances of human origin which have an amino acid sequence

substantially

present in the fibrin binding domain of

naturally-occurring human fibronectin and which are capable of

binding to fibrin.

ΙT Major Concepts

Biochemistry and Molecular Biophysics; Cardiovascular Medicine (Human

Medicine, Medical Sciences); Methods and Techniques

Chemicals & Biochemicals TΤ

fibrin; polypeptide: fibrin binding

domain, imaging agent

ANSWER 4 OF 9 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1999:9677 CAPLUS

DOCUMENT NUMBER:

130:78109

TITLE:

Application of 13C-13C, 13C-15N, and 13C-13C-15N isotopically enriched proteins as tissue-directed

image-enhancement reagents for magnetic

IT Major Concepts

Biochemistry and Molecular Biophysics; Radiology (Medical Sciences)

Chemicals & Biochemicals TT

fibrin binding domain polypeptides:

imaging agents

IT Miscellaneous Descriptors

fibrin-containing domain

ANSWER 3 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: DOCUMENT NUMBER:

2000:277499 BIOSIS PREV200000277499

TITLE:

Fibrin binding domain

polypeptides and uses and methods of producing same. Vogel, Tikv (1); Levanon, Avigdor; Werber, Moshe; Guy,

AUTHOR(S):

Rachel; Panet, Amos

CORPORATE SOURCE:

(1) Rehovot Israel

ASSIGNEE: Bio-Technology General Corp., Iselin, NJ, USA

PATENT INFORMATION: US 5965383 October 12, 1999

SOURCE:

Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 12, 1999) Vol. 1227, No. 2, pp. No

pagination. e-file.. ISSN: 0098-1133.

DOCUMENT TYPE: LANGUAGE:

Patent English

Fibrin binding domain polypeptides and uses

and methods of producing same.

This invention provides an imaging agent which comprises a polypeptide

labeled with an imageable marker, such polypeptide having an

amino acid sequence substantially present in the fibrin

binding domain of naturally-occurring human

fibronectin and being capable of binding to fibrin. The

invention further provides a method wherein the imaging agent is used for

imaging a fibrin-containing substance, i.e., a thrombus-or

atherosclerotic plaque. Further provided are plasmids for expression of polypeptides having an amino acid sequence substantially present in the

fibrin binding domain of naturally-occurring

human fibronectin and being capable of binding to fibrin

, hosts containing these plasmids, methods of producing the polypeptides, methods of treatment using the polypeptides, and methods of recovering, . . purified polypeptides substantially free of other refolding.

substances of human origin which have an amino acid sequence

substantially

present in the fibrin binding domain of

naturally-occurring human fibronectin and which are capable of binding to fibrin.

IT Major Concepts

Biochemistry and Molecular Biophysics; Cardiovascular Medicine (Human Medicine, Medical Sciences); Methods and Techniques

IT Chemicals & Biochemicals

> fibrin; polypeptide: fibrin binding domain, imaging agent

ANSWER 4 OF 9 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1999:9677 CAPLUS

DOCUMENT NUMBER:

130:78109

TITLE:

Application of 13C-13C, 13C-15N, and 13C-13C-15N isotopically enriched proteins as tissue-directed

image-enhancement reagents for magnetic

resonance imaging INVENTOR(S): Montelione, Gaetano T.; Stein, Stanley PATENT ASSIGNEE(S): University of Medicine & Dentistry of New Jersey, USA; Rutgers University SOURCE: PCT Int. Appl., 41 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: KIND DATE PATENT NO. APPLICATION NO. DATE ----------A1 19981223 WO 1998-US12568 19980617 WO 9857578 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 1998-79727 AU 9879727 A1 19990104 19980617 US 1997-878022 A 19970618 PRIORITY APPLN. INFO.: US 1997-63252 Р 19971024 WO 1998-US12568 W 19980617 REFERENCE COUNT: 3 (1) Bogdanov; US 5593658 A 1997 REFERENCE(S): (2) Brixner; US 5094848 A 1992 CAPLUS (3) Sinn; US 5308604 A 1994 CAPLUS ΤI Application of 13C-13C, 13C-15N, and 13C-13C-15N isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging Platelet (blood) IT (activated-platelet binding protein; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging) IT Nucleic acids RL: BSU (Biological study, unclassified); BIOL (Biological study) (binding proteins for; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging) MRI contrast agents IT Spin-spin relaxation (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging) TΤ Antigens Receptors RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

ΙT

Antibody conjugates

```
resonance imaging
INVENTOR(S):
                        Montelione, Gaetano T.; Stein, Stanley
                        University of Medicine & Dentistry of New Jersey,
PATENT ASSIGNEE(S):
USA;
                        Rutgers University
SOURCE:
                        PCT Int. Appl., 41 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                  KIND DATE
    PATENT NO.
                                        APPLICATION NO. DATE
     ______
                                         ----
                    A1 19981223
    WO 9857578
                                        WO 1998-US12568 19980617
        W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
            ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,
            LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
            SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG,
            KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
            FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
            CM, GA, GN, ML, MR, NE, SN, TD, TG
    AU 9879727
                                         AU 1998-79727
                     A1 19990104
                                                           19980617
PRIORITY APPLN. INFO.:
                                       US 1997-878022 A 19970618
                                       US 1997-63252
                                                       Ρ
                                                          19971024
                                       WO 1998-US12568 W 19980617
REFERENCE COUNT:
                        (1) Bogdanov; US 5593658 A 1997
REFERENCE(S):
                        (2) Brixner; US 5094848 A 1992 CAPLUS
                         (3) Sinn; US 5308604 A 1994 CAPLUS
ΤI
    Application of 13C-13C, 13C-15N, and 13C-13C-15N isotopically enriched
    proteins as tissue-directed image-enhancement reagents for
    magnetic resonance imaging
IT
    Platelet (blood)
        (activated-platelet binding protein; carbon-13-carbon-13,
        carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15
isotopically
        enriched proteins as tissue-directed image-enhancement
        reagents for magnetic resonance imaging)
IT
    Nucleic acids
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (binding proteins for; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
       tissue-directed image-enhancement reagents for magnetic
       resonance imaging)
IT
    MRI contrast agents
    Spin-spin relaxation
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
       nitrogen-15 isotopically enriched proteins as tissue-directed
       image-enhancement reagents for magnetic resonance imaging)
IT
    Antigens
    Receptors
    RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
       nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
ΙT
    Antibody conjugates
```

```
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Monoclonal antibody conjugates
TΤ
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Peptide conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Polymers, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Protein conjugates
IΤ
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Proteins (general), biological studies
ΙT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IΤ
     Organic compounds, biological studies
     Single chain antibodies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugates; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
ΙT
     Fibronectins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (fibrin-binding domain fragment;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
TΨ
     Infection
        (infectious agent antigen or receptor targeting group;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for MRI)
IT
     Proteins (specific proteins and subclasses)
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ligand-binding, nucleic acid- and protein-, conjugates;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
ΙT
     Fibrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (monoclonal antibodies to; carbon-13-carbon-13, carbon-13-nitrogen-15,
        and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
```

```
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
TΥ
     Monoclonal antibody conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
ΙT
     Peptide conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
     Polymers, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
TΤ
     Protein conjugates
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
ΙT
     Proteins (general), biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Organic compounds, biological studies
     Single chain antibodies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugates; carbon-13-carbon-13, carbon-13-nitrogen-15, and
        carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
        resonance imaging)
TΤ
     Fibronectins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (fibrin-binding domain fragment;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
ΙT
     Infection
        (infectious agent antigen or receptor targeting group;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for MRI)
IΤ
     Proteins (specific proteins and subclasses)
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ligand-binding, nucleic acid- and protein-, conjugates;
        carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-
        nitrogen-15 isotopically enriched proteins as tissue-directed
        image-enhancement reagents for magnetic resonance imaging)
IT
     Fibrins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (monoclonal antibodies to; carbon-13-carbon-13, carbon-13-nitrogen-15,
        and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as
        tissue-directed image-enhancement reagents for magnetic
```

resonance imaging) IT .beta.-Amyloid RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (plaque, targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging) ΙT Thrombus (targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging) IT Antigens RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (tumor-specific antigens; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging) IT Alzheimer's disease (.beta.-amyloid plaque targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15

carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-1: isotopically

enriched proteins as tissue-directed image-enhancement
reagents for magnetic resonance imaging)
108-77-0D, Cyanuric chloride, reaction products with tissue-directed

108-77-0D, Cyanuric chloride, reaction products with tissue-directed targeting group and isotopically enriched protein 573-58-0D, Congo red, conjugates 3934-20-1D, 2,4-Dichloropyrimidine, reaction products with tissue-directed targeting group and isotopically enriched protein 14390-96-6, Nitrogen-15, biological studies 14762-74-4, Carbon-13, biological studies 20342-94-3D, reaction products with tissue-directed targeting group and isotopically enriched protein 58626-38-3D, reaction products with tissue-directed targeting group and isotopically enriched protein 218432-70-3D, conjugates

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

IT 139639-23-9, Tissue plasminogen activator

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inactivated, conjugates; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

L9 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

ACCESSION NUMBER: 1997:244476 BIOSIS DOCUMENT NUMBER: PREV199799543679

TITLE: Recombinant polypeptides derived from the fibrin

binding domain of fibronectin

are potential agents for the imaging of blood clots. Ezov, N.; Nimrod, A.; Parizada, B.; Erber, M. M.;

AUTHOR(S): Goldlust,

A.; Greenstein, L. A.; Vogel, T.; Drizlich, N.; Levanon,

A.; Reich, S.; Gorecki, M.; Panet, A. (1)

CORPORATE SOURCE: (1) Bio-Technol. Gen., Kiryat Weizmann, Rehovot 76326

Israel

SOURCE: Thrombosis and Haemostasis, (1997) Vol. 77, No. 4, pp.

796-803.

resonance imaging)

IT .beta.-Amyloid

RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (plaque, targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

IT Thrombus

(targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (tumor-specific antigens; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

IT Alzheimer's disease

(.beta.-amyloid plaque targeting group; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15

isotopically

enriched proteins as tissue-directed image-enhancement
reagents for magnetic resonance imaging)

108-77-0D, Cyanuric chloride, reaction products with tissue-directed targeting group and isotopically enriched protein 573-58-0D, Congo red, conjugates 3934-20-1D, 2,4-Dichloropyrimidine, reaction products with tissue-directed targeting group and isotopically enriched protein 14390-96-6, Nitrogen-15, biological studies 14762-74-4, Carbon-13, biological studies 20342-94-3D, reaction products with tissue-directed targeting group and isotopically enriched protein 58626-38-3D, reaction products with tissue-directed targeting group and isotopically enriched protein 218432-70-3D, conjugates

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

IT 139639-23-9, Tissue plasminogen activator

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inactivated, conjugates; carbon-13-carbon-13, carbon-13-nitrogen-15, and carbon-13-carbon-13-nitrogen-15 isotopically enriched proteins as tissue-directed image-enhancement reagents for magnetic resonance imaging)

L9 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

ACCESSION NUMBER: 1997:244476 BIOSIS DOCUMENT NUMBER: PREV199799543679

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are potential agents for the imaging of blood clots. Ezov, N.; Nimrod, A.; Parizada, B.; Erber, M. M.;

AUTHOR(S): Goldlust,

A.; Greenstein, L. A.; Vogel, T.; Drizlich, N.; Levanon,

A.; Reich, S.; Gorecki, M.; Panet, A. (1)

CORPORATE SOURCE: (1) Bio-Technol. Gen., Kiryat Weizmann, Rehovot 76326

Israel

SOURCE: Thrombosis and Haemostasis, (1997) Vol. 77, No. 4, pp.

796-803.

ISSN: 0340-6245.

DOCUMENT TYPE: Article LANGUAGE: English

Recombinant polypeptides derived from the fibrin binding domain of fibronectin are potential agents for the imaging of blood clots.

AB Thrombus formation in the circulation is accompanied by covalent linkage of fibronectin (FN) through transglutamination of glutamine no. 3 in the fibrin binding amino terminal domain (FBD) of FN. We have exploited this phenomenon for thrombus detection by the employment

οf radioactively-labelled. . . FBD ("5 fingers"), were prepared and compared to native FN-derived 31 kDa-FBD with respect to their ability to attach to fibrin clots in vitro and in vivo. The accessibility of Gln-3 in these molecules was demonstrated by the incorporation of stoichiometric amounts of 14C-putrescine in the presence of plasma transglutaminase. Competitive binding experiments to fibrin have indicated that, although the binding affinities of the FBD molecules are lower than that of FN, substantial covalent linkage.

Miscellaneous Descriptors IT

> BLOOD AND LYMPHATIC DISEASE; BLOOD AND LYMPHATICS; FIBRIN RECOMBINANT POLYPEPTIDES; FIBRINGEN; FIBRONECTIN; INDIUM-111

LABEL; IODINE-125 LABEL; POTENTIAL BLOOD CLOT IMAGING

AGENT; RADIATION BIOLOGY; THROMBUS

ANSWER 6 OF 9 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1992:443664 CAPLUS

DOCUMENT NUMBER:

117:43664

TITLE:

Polypeptides containing the fibrin-

binding domain of

fibronectin, their recombinant production, and

their use in imaging and therapy

INVENTOR(S):

Vogel, Tikva; Levanon, Avigdor; Werber, Moshe; Guy, Rachel; Panet, Amos; Hartman, Jacob; Shaked, Hadassa

PATENT ASSIGNEE(S):

Bio-Technology General Corp., USA

SOURCE:

PCT Int. Appl., 192 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT NO.		KIND	DATE		APPLICATION NO.	DATE
WO	9117765		A1	19911128		WO 1991-US3584	19910521
	W: AU,	BR,	CA, FI,	HU, JP,	KR,	NO, SU	
	RW: AT,	ΒE,	CH, DE,	DK, ES,	FR,	GB, GR, IT, LU, NL,	SE
US	5270030		A	19931214		US 1990-526397	19900521
AU	9180760		A1	19911210		AU 1991-80760	19910521
ΑU	660618		B2	19950706			
JP	05508766		T2	19931209		JP 1991-511197	19910521
HU	66189		A2	19941028		HU 1992-3516	19910521
HU	216302		В	19990628			
ΕP	651799		A1	19950510		EP 1991-911888	19910521
ΕP	651799		B1	19990818			
	R: AT,	BE,	CH, DE,	DK, ES,	FR,	GB, GR, IT, LI, LU,	NL, SE
RU	2109750		C1	19980427		RU 1992-16360	19910521
ΑT	183545		E	19990915		AT 1991-911888	19910521

ISSN: 0340-6245.

DOCUMENT TYPE:

Article English

LANGUAGE: English
TI Recombinant polypeptides

TI Recombinant polypeptides derived from the **fibrin binding domain** of **fibronectin** are potential agents for the
imaging of blood clots.

AB Thrombus formation in the circulation is accompanied by covalent linkage of **fibronectin** (FN) through transglutamination of glutamine no. 3 in the **fibrin** binding amino terminal domain (FBD) of FN. We have exploited this phenomenon for thrombus detection by the employment

of

radioactively-labelled. . . FBD ("5 fingers"), were prepared and compared to native FN-derived 31 kDa-FBD with respect to their ability to attach to **fibrin** clots in vitro and in vivo. The accessibility of Gln-3 in these molecules was demonstrated by the incorporation of stoichiometric amounts of 14C-putrescine in the presence of plasma transglutaminase. Competitive binding experiments to **fibrin** have indicated that, although the binding affinities of the FBD molecules are lower than that of FN, substantial covalent linkage. . .

IT Miscellaneous Descriptors

BLOOD AND LYMPHATIC DISEASE; BLOOD AND LYMPHATICS; FIBRIN RECOMBINANT POLYPEPTIDES; FIBRINOGEN; FIBRONECTIN; INDIUM-111

LABEL; IODINE-125 LABEL; POTENTIAL BLOOD CLOT IMAGING

AGENT; RADIATION BIOLOGY; THROMBUS

L9 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1992:443664 CAPLUS

DOCUMENT NUMBER:

117:43664

TITLE:

Polypeptides containing the fibrin-

binding domain of

fibronectin, their recombinant production, and

their use in imaging and therapy

INVENTOR(S):

Vogel, Tikva; Levanon, Avigdor; Werber, Moshe; Guy, Rachel; Panet, Amos; Hartman, Jacob; Shaked, Hadassa

PATENT ASSIGNEE(S):

Bio-Technology General Corp., USA

SOURCE:

PCT Int. Appl., 192 pp. CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

YPE: Patent English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PAT	TENT NO.	KIND	DATE		APPLICATION NO.	DATE
WO	9117765				WO 1991-US3584	19910521
	W: AU, E	BR, CA, FI	HU, JP,	KR,	NO, SU	
	RW: AT, E	BE, CH, DE	, DK, ES,	FR,	GB, GR, IT, LU, NL,	, SE
US	5270030	Α	19931214		US 1990-526397	19900521
ΑU	9180760	A1	19911210		AU 1991-80760	19910521
ΑU	660618	В2	19950706			
JР	05508766	Т2	19931209		JP 1991-511197	19910521
HU	66189	A2	19941028		HU 1992-3516	19910521
HU	216302	В	19990628			
ΕP	651799	A1	19950510		EP 1991-911888	19910521
ΕP	651799	В1	19990818			
	R: AT, E	BE, CH, DE	DK, ES,	FR,	GB, GR, IT, LI, LU,	, NL, SE
RU	2109750	C1	19980427		RU 1992-16360	19910521
ΑT	183545	E	19990915		AT 1991-911888	19910521

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                      Α
    US 5965383
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                                          US 1997-909140
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PRIORITY APPLN. INFO.:
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                                       US 1989-345952
                                                        B2 19890428
                                       CA 1989-2006929 A 19891229
                                       US 1991-703842 B1 19910521
                                       WO 1991-US3584 A 19910521
                                       US 1993-58241 A1 19930504
                                       US 1994-259569 A3 19940614
                                       US 1995-409750
                                                        A3 19950324
    Polypeptides containing the fibrin-binding
    domain of fibronectin, their recombinant production, and
    their use in imaging and therapy
    Polypeptides having amino acid sequences substantially present in the
AΒ
    fibrin-binding domain (FBD) of human
    fibronectin are labeled with an imageable marker and
    used in imaging a thrombus or atherosclerotic plaque. Thrombolytic
    bound to the FBD polypeptides are also claimed. Wounds are treated with
    fusion products of the FBD polypeptide and a polypeptide comprising the
    cell-binding domain of human fibronectin. A human
    fibronectin cDNA library was prepd. and used in cloning and making
    various FBD polypeptides. The polypeptides were modified with DTPA and
    radiolabeled with 111In and shown to bind to preformed thrombi and
thrombi
    in vivo. They gave a high thrombus:blood ratio of 80-200 after 24 h.
The
    bacterial binding domain of fibronectin was shown to be sepd.
    from the FBD since a 31-kDa recombinant FBD polypeptide contg. the entire
    FBD (residues 1-262 of fibronectin) bound to Staphylococcus
    aureus, while 18.5 kDa and 12 kDa polypeptides contg. the 1st 154 and 109
    amino acid residues of fibronectin, resp., did not. The 18.5
    and 12 kDa polypeptides had a high covalent binding specificity for
    fibrin together with a narrower spectrum of activities and lower
    specificity for other ligands such as vascular components and bacteria
    than the 31 kDa protein which is advantageous for thrombus imaging.
ST
    fibrin binding polypeptide fibronectin imaging;
    cloning fibronectin cDNA fibrin binding protein;
    thrombus imaging fibrin binding protein; atherosclerosis plaque
    imaging
IT
    Bacteria
    Cell
    Escherichia coli
        (DNA for fibrin-binding polypeptide of human
        fibronectin cloning and expression in)
TΥ
    Plasmid and Episome
        (DNA for fibrin-binding polypeptides of human
       fibronectin on, cloning and expression of)
ΙT
    Gene, animal
    RL: BIOL (Biological study)
```

(cDNA, for fibrin-binding polypeptides of human

fibronectin, cloning and expression in Escherichia coli of)

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ES 2137928
                      Т3
                           20000101
                                         ES 1991-911888
                                                          19910521
    NO 9204405
                      Α
                           19930113
                                         NO 1992-4405
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                                          US 1995-409750
    US 5965383
                      Α
                           19991012
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    US 5869616
                      Α
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PRIORITY APPLN. INFO.:
                                                      B2 19881229
                                       US 1988-291951
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                                                       B2 19890428
                                       CA 1989-2006929 A 19891229
                                       US 1991-703842 B1 19910521
                                       WO 1991-US3584
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                                       US 1993-58241
                                                       A1 19930504
                                       US 1994-259569 A3 19940614
                                       US 1995-409750
                                                       A3 19950324
```

TI Polypeptides containing the **fibrin-binding domain** of **fibronectin**, their recombinant production, and their use in imaging and therapy

AB Polypeptides having amino acid sequences substantially present in the **fibrin-binding domain** (FBD) of human

fibronectin are labeled with an imageable marker and

used in imaging a thrombus or atherosclerotic plaque. Thrombolytic agents

bound to the FBD polypeptides are also claimed. Wounds are treated with fusion products of the FBD polypeptide and a polypeptide comprising the cell-binding domain of human **fibronectin**. A human

fibronectin cDNA library was prepd. and used in cloning and making various FBD polypeptides. The polypeptides were modified with DTPA and radiolabeled with 111In and shown to bind to preformed thrombi and thrombi

in vivo. They gave a high thrombus:blood ratio of 80--200 after 24 h. The

bacterial binding domain of **fibronectin** was shown to be sepd. from the FBD since a 31-kDa recombinant FBD polypeptide contg. the entire FBD (residues 1-262 of **fibronectin**) bound to Staphylococcus aureus, while 18.5 kDa and 12 kDa polypeptides contg. the 1st 154 and 109 amino acid residues of **fibronectin**, resp., did not. The 18.5 and 12 kDa polypeptides had a high covalent binding specificity for **fibrin** together with a narrower spectrum of activities and lower specificity for other ligands such as vascular components and bacteria than the 31 kDa protein which is advantageous for thrombus imaging.

ST fibrin binding polypeptide fibronectin imaging; cloning fibronectin cDNA fibrin binding protein; thrombus imaging fibrin binding protein; atherosclerosis plaque imaging

IT Bacteria

Cell

Escherichia coli

(DNA for fibrin-binding polypeptide of human fibronectin cloning and expression in)

IT Plasmid and Episome

(DNA for fibrin-binding polypeptides of human fibronectin on, cloning and expression of)

IT Gene, animal

RL: BIOL (Biological study)

(cDNA, for fibrin-binding polypeptides of human fibronectin, cloning and expression in Escherichia coli of)

Blood vessel, composition TΤ (components of, recombinant fibrin-binding polypeptides of human fibronectin response to) IT Thrombolytics (conjugates with fibrin-binding polypeptides of human fibronectin) IT **Fibrins** RL: BIOL (Biological study) (domain of human fibronectin binding to, labeled polypeptides contg., for imaging) Wound healing promoters IT (fibrin-binding polypeptides of human fibronectin and cell-binding polypeptides of fibronectin as) IT **Fibronectins** RL: BIOL (Biological study) (fibrin-binding polypeptides of, labeled, for imaging) IT Deoxyribonucleic acids RL: BIOL (Biological study) (for fibrin-binding polypeptides of human fibronectin , cloning and expression of) IT Anticoagulants and Antithrombotics (fusion proteins contg. fibrin-binding polypeptides of human fibronectin as) IT Thrombus and Blood clot (imaging of, with labeled fibrin-binding polypeptides of human fibronectin) Imaging TT (labeled fibrin-binding polypeptides of fibronectin for) IT Molecular cloning (of DNA for fibrin-binding polypeptides of human fibronectin on) IT Plasmid and Episome (pFN194-2, DNA for fusion protein contg. fibrin-binding and cell-binding polypeptides of human fibronectin on, cloning and expression of) IT Plasmid and Episome (pFN195-4, DNA for fusion protein contg. fibrin-binding polypeptide of human fibronectin on, cloning and expression of) ITPlasmid and Episome (pFN196-2, DNA for fibrin-binding polypeptide of human fibronectin on, cloning and expression in Escherichia coli of) IT Plasmid and Episome (pFN197-10, DNA for fibrin-binding polypeptide of human fibronectin on, cloning and expression in Escherichia coli of) IT Plasmid and Episome (pFN202-5, DNA for fusion protein contg. fibrin-binding and cell-binding polypeptides of human fibronectin on, cloning and expression of) IT Plasmid and Episome (pFN203-2, DNA for fibrin-binding polypeptide of human fibronectin on, cloning and expression in Escherichia coli of) IT Plasmid and Episome (pFN205-5, DNA for fusion protein contg. fibrin-binding polypeptide of human fibronectin on, cloning and expression in Escherichia coli of) IT Plasmid and Episome

IT Blood vessel, composition (components of, recombinant fibrin-binding polypeptides of human fibronectin response to) TT Thrombolytics (conjugates with fibrin-binding polypeptides of human fibronectin) ΙT **Fibrins** RL: BIOL (Biological study) (domain of human fibronectin binding to, labeled polypeptides contg., for imaging) IT Wound healing promoters (fibrin-binding polypeptides of human fibronectin and cell-binding polypeptides of fibronectin as) IT Fibronectins RL: BIOL (Biological study) (fibrin-binding polypeptides of, labeled, for imaging) Deoxyribonucleic acids ΙT RL: BIOL (Biological study) (for fibrin-binding polypeptides of human fibronectin , cloning and expression of) TΤ Anticoagulants and Antithrombotics (fusion proteins contg. fibrin-binding polypeptides of human fibronectin as) IT Thrombus and Blood clot (imaging of, with labeled fibrin-binding polypeptides of human fibronectin) ΙT Imaging (labeled fibrin-binding polypeptides of fibronectin for) IT Molecular cloning (of DNA for fibrin-binding polypeptides of human fibronectin on) ITPlasmid and Episome (pFN194-2, DNA for fusion protein contg. fibrin-binding and cell-binding polypeptides of human fibronectin on, cloning and expression of) IT Plasmid and Episome (pFN195-4, DNA for fusion protein contg. fibrin-binding polypeptide of human fibronectin on, cloning and expression of) IT Plasmid and Episome (pFN196-2, DNA for fibrin-binding polypeptide of human fibronectin on, cloning and expression in Escherichia coli of) IT Plasmid and Episome (pFN197-10, DNA for fibrin-binding polypeptide of human fibronectin on, cloning and expression in Escherichia coli of) IT Plasmid and Episome (pFN202-5, DNA for fusion protein contg. fibrin-binding and cell-binding polypeptides of human fibronectin on, cloning and expression of) Plasmid and Episome IT (pFN203-2, DNA for fibrin-binding polypeptide of human fibronectin on, cloning and expression in Escherichia coli of) IT Plasmid and Episome (pFN205-5, DNA for fusion protein contg. fibrin-binding polypeptide of human fibronectin on, cloning and expression in Escherichia coli of) Plasmid and Episome IT

```
(pFN208-13, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
IT
     Plasmid and Episome
        (pFN962-3, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
IT
     Extracellular matrix
     Staphylococcus aureus
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding response to)
TΤ
     Eye, disease
        (wound, treatment of, with fibrin-binding and cell-binding
        polypeptides of human fibronectin)
ΙT
     Endothelium
        (Staphylococcus aureus binding to cells of, recombinant fibrin
        -binding polypeptides of human fibronectin effect on)
TΤ
     Imaging
        (NMR, agents, paramagnetic ion conjugates with fibrin-binding
        polypeptides of human fibronectin as)
IT
     Arteriosclerosis
        (atherosclerosis, plaque, imaging of, with labeled fibrin
        -binding polypeptides of human fibronectin)
     Deoxyribonucleic acids
IΤ
     RL: BIOL (Biological study)
        (complementary, for fibrin-binding polypeptides of human
        fibronectin, cloning and expression in Escherichia coli of)
IT
     Fibrins
     RL: PROC (Process)
        (complexes, with recombinant fibrin-binding polypeptides of
        human fibronectin, characterization of)
IT
     Radioelements, compounds
     RL: BIOL (Biological study)
        (conjugates, with fibrin-binding polypeptides of human
        fibronectin, for imaging)
IT
     Scintigraphy
        (contrast agents, radioactive isotope conjugates with
        fibrin-binding polypeptides of human fibronectin as)
ΙT
     Radiography
        (contrast agents, x-ray-opaque element conjugates with fibrin
        -binding polypeptides of human fibronectin as)
ΙT
     Eye
        (cornea, epithelium, wound, treatment of, with fibrin-binding
        and cell-binding polypeptides of human fibronectin)
IT
     Eye
        (cornea, stroma, wound, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
ΙT
     Tendon
        (disease, injury, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
ΙT
     Proteins, specific or class
     RL: BIOL (Biological study)
        (fibrin-binding, labeled, of human fibronectin, for
        imaging agents)
ΙT
     Proteins, specific or class
     RL: BIOL (Biological study)
        (fusion products, of cell-binding domain and fibrin-
        binding domain polypeptides of human
        fibronectin)
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```
(pFN208-13, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
IT
     Plasmid and Episome
        (pFN962-3, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
     Extracellular matrix
ΙT
     Staphylococcus aureus
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding response to)
IT
     Burn
     Eye, disease
        (wound, treatment of, with fibrin-binding and cell-binding
        polypeptides of human fibronectin)
IT
        (Staphylococcus aureus binding to cells of, recombinant fibrin
        -binding polypeptides of human fibronectin effect on)
TΤ
     Imaging
        (NMR, agents, paramagnetic ion conjugates with fibrin-binding
        polypeptides of human fibronectin as)
IT
     Arteriosclerosis
        (atherosclerosis, plaque, imaging of, with labeled fibrin
        -binding polypeptides of human fibronectin)
IT
     Deoxyribonucleic acids
     RL: BIOL (Biological study)
        (complementary, for fibrin-binding polypeptides of human
        fibronectin, cloning and expression in Escherichia coli of)
ΙT
     Fibrins
     RL: PROC (Process)
        (complexes, with recombinant fibrin-binding polypeptides of
        human fibronectin, characterization of)
IT
     Radioelements, compounds
     RL: BIOL (Biological study)
        (conjugates, with fibrin-binding polypeptides of human
        fibronectin, for imaging)
IT
     Scintigraphy
        (contrast agents, radioactive isotope conjugates with
        fibrin-binding polypeptides of human fibronectin as)
IT
     Radiography
        (contrast agents, x-ray-opaque element conjugates with fibrin
        -binding polypeptides of human fibronectin as)
ΙT
        (cornea, epithelium, wound, treatment of, with fibrin-binding
        and cell-binding polypeptides of human fibronectin)
IT
     Eye
        (cornea, stroma, wound, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
ΙT
     Tendon
        (disease, injury, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
IT
     Proteins, specific or class
     RL: BIOL (Biological study)
        (fibrin-binding, labeled, of human fibronectin, for
        imaging agents)
IT
     Proteins, specific or class
     RL: BIOL (Biological study)
        (fusion products, of cell-binding domain and fibrin-
        binding domain polypeptides of human
        fibronectin)
```

```
IT
     Plasmid and Episome
        (pFN949-2, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
ΙT
     Plasmid and Episome
        (pFN975-25, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
IT
     Magnetic substances
        (para-, conjugates with fibrin-binding polypeptides of human
        fibronectin, for imaging)
ΙT
     Skin
        (transplant, wound in, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
IT
     Opaque materials
        (x-ray, conjugates with fibrin-binding polypeptides of human
        fibronectin, for imaging)
IT
     67-43-6D, DTPA, reaction products with recombinant fibrin
     -binding polypeptides of human fibronectin, indium-111-labeled
     142298-13-3D, DTPA reaction products, indium-111-labeled
                                                                 142298-17-7D,
     DTPA reaction products, indium-111-labeled, recombinant deriv.
     142298-19-9D, DTPA reaction products, indium-111-labeled
                                                                142298-20-2D,
     DTPA reaction products, indium-111-labeled
     RL: BIOL (Biological study)
        (atherosclerotic lesions and thrombi imaging with)
IT
     142298-11-1
     RL: BIOL (Biological study)
        (cloning of cDNA for, in recombinant fibrin-binding
        polypeptides prepn. for imaging agents)
ΙT
     142244-17-5
                   142244-18-6
     RL: PROC (Process)
        (cloning of, in recombinant fibrin-binding polypeptides
        prepn. for imaging agents)
IT
     10043-66-0D, Iodine-131, fibrin-binding polypeptide conjugates
     14119-09-6D, Gallium-67, fibrin-binding polypeptide conjugates
     14158-31-7D, Iodine-125, fibrin-binding polypeptide conjugates
     14932-42-4D, Xenon-133, fibrin-binding polypeptide conjugates
     15715-08-9D, Iodine-123, fibrin-binding polypeptide conjugates
     15750-15-9D, Indium-111, fibrin-binding polypeptide conjugates
     141517-93-3D, fusion product with fibrin-binding polypeptides of
     human fibronectin
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for imaging)
     142298-12-2, 1-109-Fibronectin (human clone pFH16/pFH134 protein
TΤ
     moiety reduced) 142298-16-6, 1-153-Fibronectin (human clone
     pFH16/pFH134 protein moiety reduced) 142298-17-7 142298-18-8, 1-154-
     Fibronectin (human clone pFH16/pFH134 protein moiety reduced)
     RL: BIOL (Biological study)
        (for imaging agent)
     14133-76-7D, Technetium-99, fibrin-binding polypeptide
     conjugates
                  15678-91-8D, fibrin-binding polypeptide conjugates,
     biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for imaging, metastable)
     141497-06-5
IT
                   141497-07-6
     RL: PRP (Properties)
        (imageable marker-labeled fibrin-binding
        polypeptides of fibronectin contg. amino-terminal sequence
        of, for imaging agents)
IT
     68181-17-9DP, N-Succinimidyl-3-(2-pyridyldithio)propionate, reaction
```

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ΙT
     Plasmid and Episome
        (pFN949-2, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
ΙT
     Plasmid and Episome
        (pFN975-25, DNA for fibrin-binding polypeptide of human
        fibronectin on, cloning and expression in Escherichia coli of)
ΙT
     Magnetic substances
        (para-, conjugates with fibrin-binding polypeptides of human
        fibronectin, for imaging)
ΙT
     Skin
        (transplant, wound in, treatment of, with fibrin-binding and
        cell-binding polypeptides of human fibronectin)
ΙT
     Opaque materials
        (x-ray, conjugates with fibrin-binding polypeptides of human
        fibronectin, for imaging)
     67-43-6D, DTPA, reaction products with recombinant fibrin
ΙT
     -binding polypeptides of human fibronectin, indium-111-labeled
     142298-13-3D, DTPA reaction products, indium-111-labeled
                                                                 142298-17-7D,
     DTPA reaction products, indium-111-labeled, recombinant deriv.
     142298-19-9D, DTPA reaction products, indium-111-labeled
                                                               142298-20-2D,
     DTPA reaction products, indium-111-labeled
     RL: BIOL (Biological study)
        (atherosclerotic lesions and thrombi imaging with)
TΤ
     142298-11-1
     RL: BIOL (Biological study)
        (cloning of cDNA for, in recombinant fibrin-binding
        polypeptides prepn. for imaging agents)
     142244-17-5
                   142244-18-6
IT
     RL: PROC (Process)
        (cloning of, in recombinant fibrin-binding polypeptides
        prepn. for imaging agents)
ΙT
     10043-66-0D, Iodine-131, fibrin-binding polypeptide conjugates
     14119-09-6D, Gallium-67, fibrin-binding polypeptide conjugates
     14158-31-7D, Iodine-125, fibrin-binding polypeptide conjugates
     14932-42-4D, Xenon-133, fibrin-binding polypeptide conjugates
     15715-08-9D, Iodine-123, fibrin-binding polypeptide conjugates
     15750-15-9D, Indium-111, fibrin-binding polypeptide conjugates
     141517-93-3D, fusion product with fibrin-binding polypeptides of
     human fibronectin
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for imaging)
     142298-12-2, 1-109-Fibronectin (human clone pFH16/pFH134 protein
ΙT
                     142298-16-6, 1-153-Fibronectin (human clone
     moiety reduced)
     pFH16/pFH134 protein moiety reduced) 142298-17-7 142298-18-8, 1-154-
     Fibronectin (human clone pFH16/pFH134 protein moiety reduced)
     RL: BIOL (Biological study)
        (for imaging agent)
TТ
     14133-76-7D, Technetium-99, fibrin-binding polypeptide
                  15678-91-8D, fibrin-binding polypeptide conjugates,
     conjugates
     biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (for imaging, metastable)
IT
     141497-06-5
                   141497-07-6
     RL: PRP (Properties)
        (imageable marker-labeled fibrin-binding
        polypeptides of fibronectin contg. amino-terminal sequence
        of, for imaging agents)
ΙT
     68181-17-9DP, N-Succinimidyl-3-(2-pyridyldithio)propionate, reaction
```

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products with recombinant fibrin-binding polypeptides of human
     fibronectin and thiolated streptokinase
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of and biol. activity of)
     80146-85-6, Transglutaminase
ΤТ
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding to fibrin clot in response to)
ΙT
     9005-49-6, Heparin, biological studies
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding to fibrin clots response to)
TΤ
     9005-49-6D, Heparin, Sepharose conjugates 9012-36-6D, Sepharose,
heparin
     conjugates
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin purifn. with)
ΙT
     9001-92-7D, Protease, conjugates with fibrin-binding
     polypeptides of human fibronectin 9002-01-1D, Streptokinase,
     conjugates with fibrin-binding polypeptides of human
                   9039-53-6D, Urokinase, conjugates with
     fibrin-binding polypeptides of human fibronectin
     81669-57-0D, Anistreplase, conjugates with fibrin-binding
     polypeptides of human fibronectin
                                        82657-92-9D, Prourokinase,
     conjugates with fibrin-binding polypeptides of human
                   139639-23-9D, conjugates with fibrin
     fibronectin
     -binding polypeptides of human fibronectin
     RL: BIOL (Biological study)
        (thrombus treatment with)
     ANSWER 7 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS
L9
                                                        DUPLICATE 3
ACCESSION NUMBER:
                    1992:44399 BIOSIS
DOCUMENT NUMBER:
                    BA93:24374
TITLE:
                    DIFFERENTIAL BEHAVIOR OF THE TWO FREE SULFHYDRYL GROUPS OF
                    HUMAN PLASMA FIBRONECTIN EFFECTS OF ENVIRONMENTAL
                    FACTORS.
                    NARASIMHAN C; LAI C S
AUTHOR(S):
CORPORATE SOURCE:
                    BIOPHYSICS SECTION, DEP. RADIOLOGY, MED. COLL. WIS., 8701
                    WATERTOWN PLANK ROAD, MILWAUKEE, WIS. 53226.
                    BIOPOLYMERS, (1991) 31 (10), 1159-1170.
SOURCE:
                    CODEN: BIPMAA. ISSN: 0006-3525.
FILE SEGMENT:
                    BA; OLD
LANGUAGE:
                    English
     DIFFERENTIAL BEHAVIOR OF THE TWO FREE SULFHYDRYL GROUPS OF HUMAN PLASMA
     FIBRONECTIN EFFECTS OF ENVIRONMENTAL FACTORS.
AB
     We report here a novel approach to label specifically one of the
     two cryptic, free sulfhydryl groups per subunit of human plasma
     fibronectin with either an 15N, 2H-maleimide spin label
     or a coumarinylphenyl maleimide fluorescent label. This permits
     the use of electron spin resonance (ESR) or fluorescence techniques to
     study molecular dynamics of fibronectin with the label
     attached to a single site per chain on the protein molecule. The method
is
     based on our observation that upon adsorption of fibronectin to
     a gelatin-coated surface, the SH1 site, located between the DNA-binding
     and the cell-binding domains, is partially exposed, while the SH2 site,
     located within the carboxyl-terminal fibrin-binding
```

```
products with recombinant fibrin-binding polypeptides of human
     fibronectin and thiolated streptokinase
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of and biol. activity of)
     80146-85-6, Transglutaminase
IT
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding to fibrin clot in response to)
     9005-49-6, Heparin, biological studies
TΨ
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin binding to fibrin clots response to)
IT
     9005-49-6D, Heparin, Sepharose conjugates 9012-36-6D, Sepharose,
heparin
     conjugates
     RL: BIOL (Biological study)
        (recombinant fibrin-binding polypeptides of human
        fibronectin purifn. with)
     9001-92-7D, Protease, conjugates with fibrin-binding
IT
     polypeptides of human fibronectin 9002-01-1D, Streptokinase,
     conjugates with fibrin-binding polypeptides of human
     fibronectin
                   9039-53-6D, Urokinase, conjugates with
     fibrin-binding polypeptides of human fibronectin
     81669-57-0D, Anistreplase, conjugates with fibrin-binding
     polypeptides of human fibronectin
                                        82657-92-9D, Prourokinase,
     conjugates with fibrin-binding polypeptides of human
                   139639-23-9D, conjugates with fibrin
     fibronectin
     -binding polypeptides of human fibronectin
     RL: BIOL (Biological study)
        (thrombus treatment with)
     ANSWER 7 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS
L9
                                                        DUPLICATE 3
ACCESSION NUMBER:
                    1992:44399 BIOSIS
DOCUMENT NUMBER:
                    BA93:24374
                    DIFFERENTIAL BEHAVIOR OF THE TWO FREE SULFHYDRYL GROUPS OF
TITLE:
                    HUMAN PLASMA FIBRONECTIN EFFECTS OF ENVIRONMENTAL
                    FACTORS.
                    NARASIMHAN C; LAI C S
AUTHOR(S):
CORPORATE SOURCE:
                    BIOPHYSICS SECTION, DEP. RADIOLOGY, MED. COLL. WIS., 8701
                    WATERTOWN PLANK ROAD, MILWAUKEE, WIS. 53226.
                    BIOPOLYMERS, (1991) 31 (10), 1159-1170.
SOURCE:
                    CODEN: BIPMAA. ISSN: 0006-3525.
FILE SEGMENT:
                    BA; OLD
LANGUAGE:
                    English
     DIFFERENTIAL BEHAVIOR OF THE TWO FREE SULFHYDRYL GROUPS OF HUMAN PLASMA
     FIBRONECTIN EFFECTS OF ENVIRONMENTAL FACTORS.
AΒ
     We report here a novel approach to label specifically one of the
     two cryptic, free sulfhydryl groups per subunit of human plasma
     fibronectin with either an 15N, 2H-maleimide spin label
     or a coumarinylphenyl maleimide fluorescent label. This permits
     the use of electron spin resonance (ESR) or fluorescence techniques to
     study molecular dynamics of fibronectin with the label
     attached to a single site per chain on the protein molecule. The method
is
     based on our observation that upon adsorption of fibronectin to
     a gelatin-coated surface, the SH1 site, located between the DNA-binding
     and the cell-binding domains, is partially exposed, while the SH2 site,
     located within the carboxyl-terminal fibrin-binding
```

domain, remains buried and unreactive. The procedures for the preparation of the selectively labeled fibronectins are described in detail. The physicochemical properties of these single-site labeled fibronectins, particularly as affected by high salt, heparin, surface binding, and temperature, were characterized by ESR spin-label and steady-state fluorescence techniques. The steady-state fluorescence measurement indicates that both local environments of SH1 and SH2 sites are relatively. . . increase in the domainal flexibility in both SH1 and SH2 regions, perhaps through the disruption of domain-domain interactions in the fibronectin molecule, and that the former is more effective than the latter in producing such an effect. The observed heparin effect. . . processes. The data presented here suggest that the newly developed method for differential labeling of the free sulfhydryl groups in fibronectin should be useful for mapping the spatial arrangement of structural

in the protein molecule using spin-label-spin-probe and fluorescene energy transfer techniques.

ANSWER 8 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4

1989:444158 BIOSIS ACCESSION NUMBER:

BA88:92430 DOCUMENT NUMBER:

EVIDENCE THAT THE TWO FREE SULFHYDRYL GROUPS OF PLASMA TITLE:

FIBRONECTIN ARE IN DIFFERENT LOCAL ENVIRONMENTS

SATURATION-RECOVERY ESR STUDY.

LAI C-S; NARASIMHAN C; YIN J-J AUTHOR(S):

CORPORATE SOURCE: NATL. BIOMED. ESR CENT., DEP. RADIOL., MED. COLL.

WISCONSIN, 8701 WATERTOWN PLANK RD, MILWAUKEE, WIS.

523226.

SOURCE: BIOPHYS J, (1989) 56 (2), 396-400.

CODEN: BIOJAU. ISSN: 0006-3495.

FILE SEGMENT: BA; OLD LANGUAGE: English

EVIDENCE THAT THE TWO FREE SULFHYDRYL GROUPS OF PLASMA FIBRONECTIN TIARE IN DIFFERENT LOCAL ENVIRONMENTS SATURATION-RECOVERY ESR STUDY.

Human plasma fibronectin is a dimer consisting of two subunits; each contains two cryptic thiol groups that were selectively labeled with an 15N,2H-maleimide spin label. Previous studies using conventional X-band electron spin resonance (ESR) methods showed that the spectrum of the labeled protein displays a. . . which was deconvoluted into two T1 values of 1.37 and 4.53 .mu.s. Thus, the two spin-labeled sulfhydryl sites of plasma fibronectin (Fn), being similar in rates of rotational diffusion, differ by a factor of 3.2 in T1. Parallel experiments using various fibronectin fragments showed that the 1.37-.mu.s component is associated with the label attached onto the thiol located in between the DNA-binding and the cell-binding domains.

and the 4.53-.mu.s component is associated with the label attached onto the thiol located within the carboxyl-terminal fibrin-binding domain. The data suggest that the saturation-recovery ESR is a useful method for differentiating multiple spin-labeled sites on macromolecules in which the labels undergo similar rates of rotational motion.

ANSWER 9 OF 9 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1989:511284 CAPLUS

DOCUMENT NUMBER: 111:111284

Evidence that the two free sulfhydryl groups of TITLE:

plasma

domain, remains buried and unreactive. The procedures for the preparation of the selectively labeled fibronectins are described in detail. The physicochemical properties of these single-site labeled fibronectins, particularly as affected by high salt, heparin, surface binding, and temperature, were characterized by ESR spin-label and steady-state fluorescence techniques. The steady-state fluorescence measurement indicates that both local environments of SH1 and SH2 sites are relatively. . . increase in the domainal flexibility in both SH1 and SH2 regions, perhaps through the disruption of domain-domain interactions in the fibronectin molecule, and that the former is more effective than the latter in producing such an effect. The observed heparin effect. . . processes. The data presented here suggest that the newly developed method for differential labeling of the free sulfhydryl groups in fibronectin should be useful for mapping the spatial arrangement of structural

in the protein molecule using spin-label-spin-probe and fluorescene energy transfer techniques.

L9 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4

ACCESSION NUMBER: 1989:444158 BIOSIS

DOCUMENT NUMBER: BA88:92430

TITLE: EVIDENCE THAT THE TWO FREE SULFHYDRYL GROUPS OF PLASMA

FIBRONECTIN ARE IN DIFFERENT LOCAL ENVIRONMENTS

SATURATION-RECOVERY ESR STUDY.

AUTHOR(S): LAI C-S; NARASIMHAN C; YIN J-J

CORPORATE SOURCE: NATL. BIOMED. ESR CENT., DEP. RADIOL., MED. COLL.

WISCONSIN, 8701 WATERTOWN PLANK RD, MILWAUKEE, WIS.

523226.

SOURCE: BIOPHYS J, (1989) 56 (2), 396-400.

CODEN: BIOJAU. ISSN: 0006-3495.

FILE SEGMENT: BA; OLD LANGUAGE: English

TI EVIDENCE THAT THE TWO FREE SULFHYDRYL GROUPS OF PLASMA FIBRONECTIN ARE IN DIFFERENT LOCAL ENVIRONMENTS SATURATION-RECOVERY ESR STUDY.

AB Human plasma fibronectin is a dimer consisting of two subunits; each contains two cryptic thiol groups that were selectively labeled with an 15N,2H-maleimide spin label. Previous studies using conventional X-band electron spin resonance (ESR) methods showed that the spectrum of the labeled protein displays a. . . which was deconvoluted into two Tl values of 1.37 and 4.53 .mu.s. Thus, the two spin-labeled sulfhydryl sites of plasma fibronectin (Fn), being similar in rates of rotational diffusion, differ by a factor of 3.2 in Tl. Parallel experiments using various fibronectin fragments showed that the 1.37-.mu.s component is associated with the label attached onto the thiol located in between the DNA-binding and the cell-binding domains,

and the 4.53-.mu.s component is associated with the label attached onto the thiol located within the carboxyl-terminal fibrin-binding domain. The data suggest that the saturation-recovery ESR is a useful method for differentiating multiple spin-labeled sites on macromolecules in which the labels undergo similar rates of rotational motion.

L9 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1989:511284 CAPLUS

DOCUMENT NUMBER: 111:111284

TITLE: Evidence that the two free sulfhydryl groups of

plasma

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                         environments. Saturation-recovery electron spin
                         resonance study
                         Lai, Ching San; Narasimhan, C.; Yin, Jun Jie
AUTHOR(S):
                         Natl. Biomed. Electron Spin Reson. Cent., Med. Coll.
CORPORATE SOURCE:
                         Wisconsin, Milwaukee, WI, 53226, USA
                         Biophys. J. (1989), 56(2), 395-400
SOURCE:
                         CODEN: BIOJAU; ISSN: 0006-3495
DOCUMENT TYPE:
                         Journal
                         English
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     each contains 2 cryptic SH groups that were selectively labeled with an
     15N, 2H-maleimide spin label. Satn.-recovery ESR was used to
     measure directly electron spin-lattice relaxation time (T1) of the
     protein in soln. at 27.degree.. Interestingly, the time evolution of the
     signal was biphasic, which was deconvoluted into 2 T1 values of 1.37 and
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                                       The
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     spin-labeled sites on macromols. in which the labels undergo
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ST
     fibronectin sulfhydryl ESR
IΤ
     Blood plasma
        (fibronectins of, multiple sulfhydryl groups of, ESR study
        of)
     Macromolecular compounds
TT
     RL: BIOL (Biological study)
        (multiple spin label studies of, satn.-recovery ESR for)
IT
    Mercapto group
        (of fibronectin, of human blood plasma, multiple sites of,
        ESR study of)
IT
     Electron spin resonance spectrometry
        (of macromols. contg. multiple spin labels, rotational motion
        in relation to)
ΙT
     Fibronectins
     RL: PRP (Properties)
        (sulfhydryl groups of, of human blood plasma, multiple sites of, ESR
        study of)
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     (FILE 'HOME' ENTERED AT 16:23:05 ON 02 NOV 2001)
     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, SCISEARCH' ENTERED AT 16:24:37 ON
     02 NOV 2001
L1
         100222 S FIBRONECTIN
            198 S FIBRIN (W) BINDING (W) DOMAIN
1.2
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                         environments. Saturation-recovery electron spin
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     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, SCISEARCH' ENTERED AT 16:24:37 ON
     02 NOV 2001
L1
         100222 S FIBRONECTIN
L2
            198 S FIBRIN (W) BINDING (W) DOMAIN
```

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L3 135 S L1 AND L2
L4 6568 S L1 AND (MARKER OR IMAGE OR ISOTOPE OR LABEL)
L5 149 S L4 AND FIBRIN
L6 15 S L5 AND ((THROMBUS OR ATHEROSCLEROTIC (W) PLAQUE))
L7 17 S L5 AND ((FIBRIN (W) BINDING (W) DOMAIN))
L8 11 DUP REM L6 (4 DUPLICATES REMOVED)
L9 9 DUP REM L7 (8 DUPLICATES REMOVED)
```

=> log off y

STN INTERNATIONAL LOGOFF AT 16:49:18 ON 02 NOV 2001

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L3 135 S L1 AND L2
L4 6568 S L1 AND (MARKER OR IMAGE OR ISOTOPE OR LABEL)
L5 149 S L4 AND FIBRIN
L6 15 S L5 AND ((THROMBUS OR ATHEROSCLEROTIC (W) PLAQUE))
L7 17 S L5 AND ((FIBRIN (W) BINDING (W) DOMAIN))
L8 11 DUP REM L6 (4 DUPLICATES REMOVED)
L9 9 DUP REM L7 (8 DUPLICATES REMOVED)
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=> log off y

STN INTERNATIONAL LOGOFF AT 16:49:18 ON 02 NOV 2001